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E. MERCK'S

ANNUAL REPORT

:: OF RECENT ADVANCES IN ::
PHARMACEUTICAL CHEMISTRY
:: AND THERAPEUTICS ::

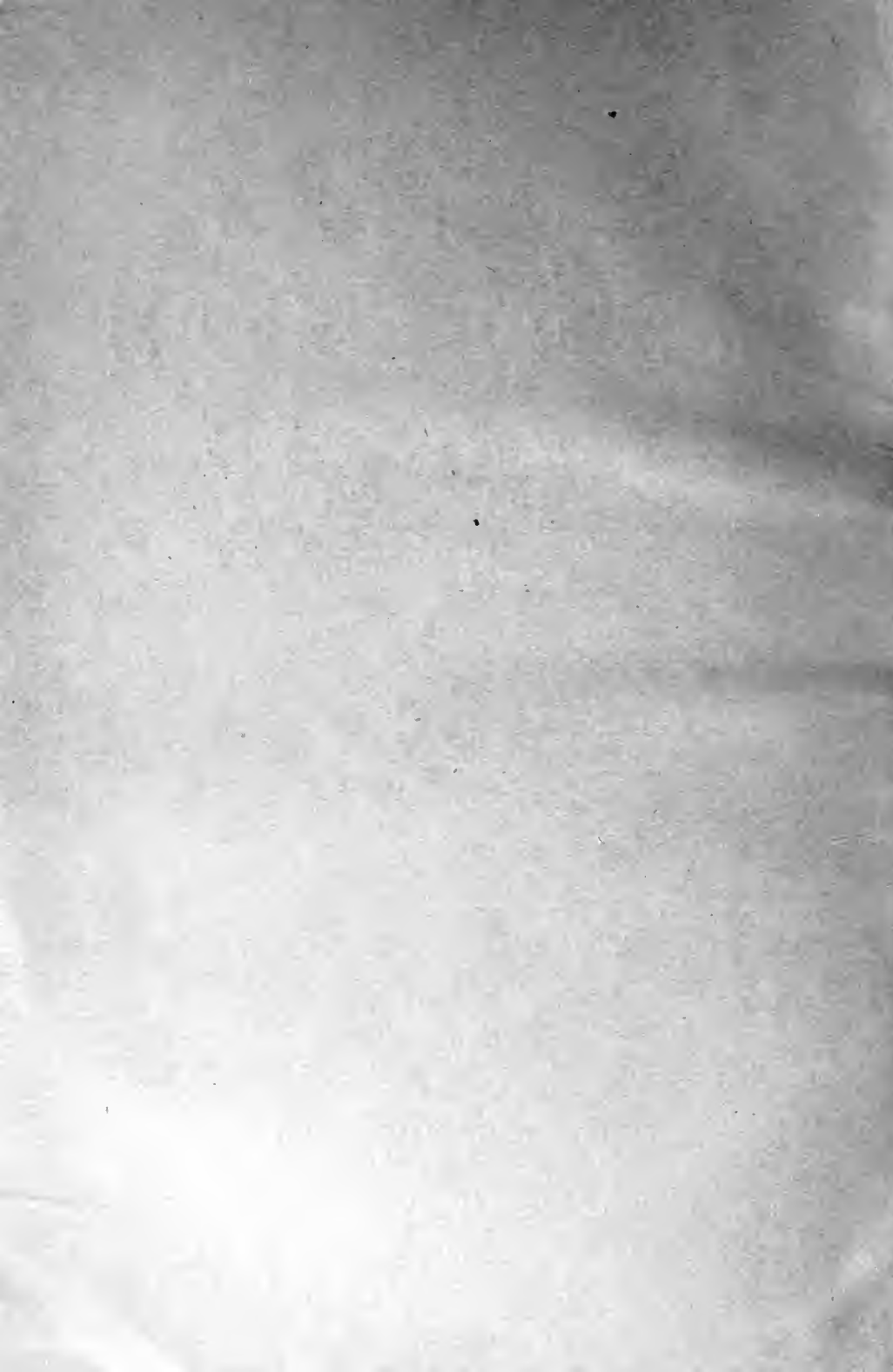
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1913 :: VOLUME XXVII

E. MERCK, CHEMICAL WORKS, DARMSTADT

1914



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ANNUAL REPORT

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Nuclein and Nucleinic Acid.

Nuclein and lecithin, two compounds of phosphorus of considerable biological importance to the plant and animal organism, have for many years past engaged the attention of therapeutists. Lecithin was dealt with in my Annual Report for 1912; the following notes are devoted to a consideration of nuclein and nucleinic acid.

In the first place, it is necessary to establish a clear definition of the terms nuclein and nucleinic acid, as I have found from experience that both terms are sometimes regarded as synonymous. Particularly the term nuclein is frequently employed instead of nucleinic acid, probably because the former is the shorter expression. Nuclein, however, as yet occupies a relatively unimportant place in therapeutics, and it is nucleinic acid which during the past few years has grown in medical interest.

The statement made above regarding the importance of nuclein to the organism must be taken *cum grano salis*, for in the living cell, or rather in the nucleus which is so closely connected with cell-division, no nuclein, but a nucleo-proteid is present. The nucleins are degradation products of the nucleo-proteids, and are formed from the latter, *inter alia*, by the splitting off of albumin, e. g., by digesting with pepsin - hydrochloric acid. The nucleo - proteids are first of all converted into nucleins, and after giving up more albumin, into nucleinic acids. The chemical relationship of these bodies may be represented as follows: nucleinic acid in combination with one part of albumin forms a nuclein, and with two parts of albumin, a nucleo-proteid. As the nucleins never occur as such in the nucleus, but are to a certain extent artificial products*, Hammarsten suggested the rejection of the term "nucleins" in favour of the expression "denaturated nucleo-proteids". In the foregoing the term "nuclein" has been defined with sufficient clearness; however, it must be borne in mind that there are so-called "pseudo-nucleins" (para-nucleins), substances containing phosphorus and resembling the real nucleins, which are produced by the peptic digestion

* Compare Oppenheimer, *Handbuch der Biologie* 1909, Vol. 1, p. 601.
Hammarsten, *Lehrbuch der physiologischen Chemie*.

of other albuminous bodies containing phosphorus, but which on further decomposition do not yield nucleinic acid since they do not contain a nucleinic acid group.

Nothing definite can be said with regard to the molecular composition of the nucleins, and only attempts have been made to establish a formula for the nucleinic acids. Thus, Steudel attributes to nucleinic acid a (thymus nucleinic acid) the formula $C_{43}H_{57}N_{15}O_{30}P_4$, Schmiedeberg the formula $C_{40}H_{56}N_{14}O_{16}, 2P_2O_5$, Kostytschew the formula $C_{41}H_{74}N_{14}O_{26}P_4$, and Kowalewsky the formula $C_{29}H_{42}N_{13}O_{23}P_3$. As nucleinic acid b is more soluble in water, Schmiedeberg assumes that it is a hydrate of nucleinic acid a, and Kostytschew gives it the formula $C_{90}H_{153}N_{27}O_{61}P_{10}$.

The degradation products of the nucleinic acids are very characteristic, and have been studied and described by Kossel, Neumann, Steudel, and others. Of these, up to the present, the following have been isolated: purin bases, such as adenine, guanine, hypoxanthine and xanthine; pyrimidine bases, such as cytosine, thymine and uracil; carbohydrates, probably pentoses or hexoses; and phosphoric acid. As is the case in lecithin, phosphoric acid appears to form the nucleus of the molecule in the nucleins and nucleinic acids, but a structural formula of nucleinic acid cannot be established. Burian and Steudel have attempted to throw light upon

Steudel, Zeitschrift für physiologische Chemie 1907, Vol. 53, p. 14.
Schmiedeberg, Archiv für experimentelle Pathologie 1907, Vol. 57, p. 329.

Kostytschew, Zeitschrift für physiologische Chemie 1903, Vol. 39, p. 545.

Kowalewsky, ibidem 1910, Vol. 69, p. 240.

Kossel, Zeitschrift für physiologische Chemie 1881, Vol. 5, p. 152, 267; 1882, Vol. 6, p. 431; 1883, Vol. 7, p. 7; 1883/84, Vol. 8, p. 404; 1884, Vol. 10, p. 248; 1888, Vol. 12, p. 241; Berichte der deutschen chemischen Gesellschaft Berlin 1885, Vol. 18, p. 79 and 1928; 1894, Vol. 27, p. 2215; du Bois-Reymonds Archiv 1891, p. 181, 1894, p. 551.

Kossel-Neumann, Berichte der deutschen chemischen Gesellschaft 1893, Vol. 26, p. 2753; Archiv für Anatomie und Physiologie 1894, p. 194.

Steudel, Zeitschrift für physiologische Chemie 1907, Vol. 50, p. 538 and Vol. 52, p. 62.

Burian, Berichte der deutschen chemischen Gesellschaft 1904, Vol. 37, p. 708; Zeitschrift für physiologische Chemie 1904, Vol. 42, p. 297; 1907, Vol. 51, p. 425.

Steudel, Zeitschrift für physiologische Chemie 1906, Vol. 48, p. 425.

this point, and those interested in this question should consult their publications. The definition of the terms nucleins and nucleinic acids may be summarized as follows:

Nucleins are albuminous compounds containing phosphorus, which are produced by the artificial decomposition of the nucleo-proteids and which contain a nucleinic acid group.

Nucleinic acids are organic acids containing phosphorus and nitrogen, in which, in addition to phosphoric acid in (probably) ester-like combination, purin bases, carbohydrates and sometimes pyrimidine bases are also present. They are produced from the nucleo-proteids by the complete dissociation of albumins.

With regard to the history of nucleins and of nucleinic acid it may be mentioned that F. Miescher was the first to isolate and describe a nucleinic acid, obtained from the sperm of salmon. The term nucleinic acid was applied later to this substance, when R. Altmann had established its acid nature. According to Miescher, nucleinic acid was prepared by a large number of investigators, by A. Noll, W. Gulewitsch, P. Levene, C. Alsberg and K. Inouye from the sperm or the eggs of various fishes, by A. Neumann from the spleen and pancreas, by J. Lonnberg from the kidneys, and by P. Levene from the spleen, pancreas, testicles, kidneys, liver, brain, etc. Special methods of preparation have been described by Neumann and Schmiedeberg. Nuclein was prepared by Miescher in 1869 from the nuclei of pus cells and later from salmon sperm; further

Miescher, *Archiv für experimentelle Pathologie* 1895, Vol. 37, p. 100.

Altmann, *Archiv für Anatomie und Physiologie* 1889, p. 524.

Noll, *Zeitschrift für physiologische Chemie* 1899, Vol. 25, p. 430.

Gulewitsch, *ibidem* 1899, Vol. 27, p. 292.

Levene, *ibidem* 1901, Vol. 32, p. 541 and 1907, Vol. 50, p. 1.

Alsberg, *Archiv für experimentelle Pathologie* 1904, Vol. 51, p. 239.

Inouye, *Zeitschrift für physiologische Chemie* 1906, Vol. 48, p. 181.

Neumann, *Archiv für Anatomie und Physiologie* 1899, Supplement, p. 552.

Lonnberg, *Skandinavisches Archiv für Physiologie* Vol. 3, p. 1.

Levene, *Zeitschrift für physiologische Chemie* 1901, Vol. 32, p. 541;

1902/03, Vol. 37, p. 402; 1903, Vol. 38, p. 80; Vol. 39, p. 479;

1904, Vol. 41, p. 404; Vol. 43, p. 199; 1905, Vol. 46, p. 155;

1906, Vol. 47, p. 140 and Vol. 49, p. 262.

Miescher, *Hoppe-Seylers medizinisch-chemische Untersuchungen* p. 441; *Archiv für experimentelle Pathologie* 1896, Vol. 37, p. 148.

by Mathews from the sperm of herrings, by von Jaksch from the human brain, by Ploss from the red blood corpuscles, by Lubawin from raw milk casein, and by Hoppe-Seyler and Kossel from beer yeast.

The following remarks are devoted to a description of the preparations issued by me.

Nuclein.

I supply two nucleins, a nuclein prepared from beer yeast, and a nuclein according to Horbaczewski. The former, as indicated by its name, is prepared by a special process from beer yeast, and occurs as a light brown, amorphous powder. It is completely soluble only in dilute alkalies with partial dissociation of albumin and formation of a nucleinate. It is slightly soluble in water, still less soluble in mineral acids; it is insoluble in ether and alcohol. The second preparation is obtained according to the directions of Horbaczewski from spleen pulp. It is a greyish-brown powder, soluble in dilute alkalies. Both preparations may be used in the same way for therapeutic purposes.

Chemical tests for establishing the purity of nucleins have not yet been elaborated, as the chemical structure of these bodies still awaits investigation and the correlation between the albumin, or nitrogen, and the phosphoric acid content of the various nucleins is not known. The recognition of the identity must be confined to determining the solubility of the nuclein, and demonstrating the presence of phosphorus and sulphur by destroying the nuclein by heating with soda and potassium nitrate; the resulting mass is dissolved in water, the solution acidified by the addition of nitric acid, and tested with molybdate solution for phosphoric acid, and with solution of barium nitrate for sulphuric acid*. It may

Mathews, Zeitschrift für physiologische Chemie 1897, Vol. 23, p. 406.

Jaksch, Pflügers Archiv für Physiologie 1876, Vol. 13, p. 469.

Ploss, Hoppe-Seylers medizinisch-chemische Untersuchungen p. 463.

Lubawin, ibidem p. 486.

Hoppe-Seyler, ibidem p. 416, 500.

Kossel, Zeitschrift für physiologische Chemie 1879, Vol. 3, p. 284.

Horbaczewski, Monatshefte für Chemie 1891, Vol. 12, p. 225.

* Compare Kossel, Zeitschrift für physiologische Chemie, Vol. 7, p. 7.

be mentioned that the nucleins give the biuret reaction and also the pentose reaction (Tollens' orcin reaction).

The physiological importance of the nucleins to the organism is especially apparent from the fact that the nucleins, and the nucleo-proteids, are widely distributed in the plant and animal organism. It finds a further confirmation in the fact that the nucleus, which is indispensable to cell life, is largely composed of nucleo-proteids. The bases adenine, guanine, hypoxanthine and xanthine present in the cells and tissues probably owe their origin to nucleins. Whether the nucleo-proteids are formed in the organism from phosphates and albuminous compounds, or whether they are introduced in an unaltered form by absorption from the nucleo-proteids present in food, is as yet not established. It is probable, but has not yet been demonstrated, that the nucleo-proteids contained in vegetable and animal foods are more or less broken down in the digestive tract and absorbed in the form of nucleinic acid, and beyond the intestine nucleins and nucleo-proteids are again formed from the nucleinic acid and the albuminous compounds present in the various tissues. At least it has been experimentally demonstrated* that albumins and nucleinic acid in an aqueous solution yield insoluble nucleo-proteids. It may also be assumed that the decomposition of nuclein in the intestine goes further than its resolution into nucleinic acid and that its degradation products (see above) unite again to form nucleo-proteids beyond the intestine. The experiments of Gumlich and Popoff show that absorption of nuclein from the food takes place. Gumlich found that after feeding with nuclein the phosphorus content of the urine increased, while Popoff was able to demonstrate that of the nucleins introduced into the body only a relatively small amount went into solution in the stomach, whereas a considerable amount was dissolved in the intestine by the action of the pancreatic juice. According to the results of this author's experiments, it would appear as if the nucleins were present in this solution in an unaltered form, in which case the view expressed above to the effect that nucleins are absorbed in the form of nucleinic acid or

* Compare Altmann and Milroy.

Gumlich, *Zeitschrift für physiologische Chemie* 1894, Vol. 18, p. 508.

Popoff, *ibidem* 1894, Vol. 18, p. 532.

of sodium nucleinate receives a certain amount of support. The increase in the phosphoric acid content of the urine, observed by Gumlich, suggests that a part of the phosphoric acid in urine is derived from the nucleins contained in food. Uric acid is produced directly or indirectly, by way of the nuclein bases, in the dissociation of phosphoric acid from the nucleins in the organism. According to various investigators, including Gumlich, Stadthagen and Weintraud, the amount of uric acid excreted is indicative of the nuclein metabolism which has taken place in the organism.

Nuclein was introduced into therapeutics by Horbaczewski in 1892. This investigator had found that nuclein possesses pronounced pyrogenic properties, and is also capable of powerfully stimulating leucocytosis. This action was confirmed by M. Hahn, who was able to demonstrate that the number of leucocytes in the blood was doubled by the introduction of nuclein, and also that the defibrinated blood obtained during the stage of hyperleucocytosis had a very considerably greater bactericidal action than the normal blood of the same experimental animal. In common with almost all investigators who have studied nuclein therapy in the treatment of infectious diseases, he starts from the assumption that the bactericidal effect of blood increases with the number of leucocytes. It was therefore to a certain extent justifiable to try the use of nuclein as a leucocytactic agent in combating pathogenic bacteria in infectious diseases. The fact must not be overlooked that already prior to the use of nuclein this substance was employed in the form of spleen pulp to stimulate leucocytosis, as is apparent from the results of Goldscheider's experiments.

In his therapeutic experiments Horbaczewski prescribed the nuclein obtained from spleen pulp (nuclein according to Horbaczewski). In chronic varicose ulcers of the leg doses of 2 to 5 grammes (30—75 grains) proved extremely useful, and in lupus gave rise to reactions resembling those follow-

Stadthagen, Virchows Archiv Vol. 109, p. 417.

Weintraud, Archiv für Anatomie und Physiologie 1895, p. 382.

Horbaczewski, Allgemeine Wiener medizinische Zeitung 1892, Merck's Report 1896, p. 102.

Hahn, Berliner klinische Wochenschrift 1896, No. 39, p. 864.

Goldscheider, Zeitschrift für klinische Medizin Vol. 25, Merck's Report 1908, p. 67.

ing the use of tuberculin. For this reason Germain Sée employed it in pulmonary tuberculosis, and in five cases of masked tuberculosis he observed that it caused a rise of temperature and cavernous râles were audible, thus making it possible to detect hitherto unsuspected foci of infection. In inflammation of the lungs doses of 2 to 3 grammes (30—45 grains), administered per os for four or five days, also led to a definite improvement.

H. Mourek continued Horbaczewski's experiments in lupus, but with this difference that he administered nuclein by hypodermic injection. For this purpose he dissolved 2.5 grammes of nuclein according to Horbaczewski in a little water, adding drop by drop solution of sodium hydroxide (0.5 p. c.), with constant rubbing, and after the addition of 2.5 grammes of phenol the solution was made up to 500 c. c. with water and then filtered. This solution, which he found remained unaltered for a considerable time, contains 0.005 gramme of nuclein in 1 c. c. At first he injected 0.5 c. c. daily and gradually increased the dose by 0.5 c. c. up to 12 c. c. Before increasing the dose he always waited until the general reaction had subsided and the patient reacted more markedly to a certain dose. With this medication he never observed habituation or the occurrence of violent or threatening symptoms. The general reaction in most cases consisted in a rise in temperature (on an average up to 38° C.), which disappeared after a day or two. Vomiting, loss of appetite and cardialgia never occurred, but sometimes headache and depression were observed. The urine showed no change. An increase in the eosinophiles took place only after the disappearance of the fever. Usually, there was an increase in body-weight. The local reaction consisted in redness and swelling of the infected parts associated with slight pain and a little tension in the affected areas. The author did not obtain a cure, but an appreciable objective improvement, and he sums up his view of nuclein as follows: "Nuclein is a pyrogenic substance which displays a fairly mild action when administered internally, whereas hypodermic injection is followed by a more violent effect. — It assists and stimulates the formation of leucocytes and thus causes leucocyto-

Sée, *Semaine médicale* 1893, p. 227.

Mourek, *Wiener medizinische Wochenschrift* 1893, No. 35 and 36.

sis. — It causes an increase in the chronic inflammatory processes.”

Sommers expressed himself in the following terms with regard to nuclein: Nuclein, which is deposited by the leucocytes in the cells in the organism, is the carrier of the antitoxic properties of the organism and its therapeutic use has frequently yielded good results in carcinoma, tuberculosis, pernicious anæmia, angina, diphtheria, marasmus, cachexia, and inflammatory infectious and asthenic processes*. He recommends the internal administration of the preparation in the form of powders or tablets. For this purpose the following prescriptions may be used:

Rp. Nuclein (from yeast) 5 grammes (75 grains)

Divide in part. æqual. X.

Sig.: 4 to 6 powders daily.

Rp. Nuclein Horbaczewski 5 grammes (75 grains)

Sacchar. 10 „ (150 „)

Mucilag. acac. q. s. ut f. tabulett. XX.

Sig.: 5 to 10 tablets daily.

E. de Renzi made experiments with parenchymatous injections in tuberculosis. As an initial dose he injected 0.5 c.c. (of Mourek's solution) daily, gradually increasing the amount by 0.25 c.c. up to a dose of 3.25 c.c. The injections did not give rise to any local or general disturbances, only in one patient a feeling of lassitude and slight headache occurred during treatment. In four other cases the remedy was well borne. Of the five persons who were treated by this method three showed a definite improvement of the general condition, and in one patient a decrease in the cavernous râles was also observed; however, in no case did he obtain a striking result by this treatment. Nevertheless, the author was able to observe an increase in the number of leucocytes in the blood of the patients treated with nuclein.

Sommers (New York), *Therapeutische Wochenschrift* 1895, p. 604.

* Compare also: J. Aulde, *New York Medical Journal* 1894, No. 12; Garber, *Therapeutic Gazette* 1895, January; M. O. Teigen, *Therapeutic Gazette* 1895, June; Wilcox, *Therapeutic Gazette* 1895, August; V. Vaughan, *American Medical and Surgical Bulletin* 1896, p. 641; Hugh C. Ross and Ch. Macalister, *British Medical Journal* 1909, II., p. 1217.

Renzi, *Therapeutische Wochenschrift* 1895, p. 721.

A contribution by J. Hofbauer dealing with the value of nuclein in septic puerperal infections throws an interesting light on nuclein therapy in infectious diseases. Based on the favourable effect of hyperleucocytosis in infections, he made use of nuclein Horbaczewski to produce this effect, because this preparation, administered per os, displays a prompt leucocytactic action and is free from any unwelcome by-effects. His assumption was further strengthened by the fact, demonstrated by Popoff, that nuclein administered by mouth is split up into nucleinic acid under the influence of the pancreatic juice, and is present in this form in the chyme, from which it passes into the blood circulation. He also draws attention to the results obtained by Tichomiroff, Vaughan and Kossel, which show that nucleinic acid precipitates the toxalbumins produced by bacteria, and displays a bactericidal action even in dilute solutions. He records the following results.

The general condition of the patients to whom nuclein was administered showed a striking improvement. Even patients with a high temperature appeared fresher and assumed a more tranquil expression, they became less apathetic and the icteric colouring of the face, as well as the loss of appetite, disappeared. The crusts on the ulcera puerperalia were thrown off and the latter very quickly formed healthy granulating surfaces which were soon covered by a layer of epithelium. The offensive odour of the endometritic secretion often disappeared within a few hours, and the purulent secretion which then followed rapidly diminished, so that the intra-uterine injections could soon be replaced by vaginal douches containing a mild disinfectant. The influence of nuclein on the temperature was apparent within the first twelve to twenty-four hours, causing a considerable rise, but during the following days the cases running a favourable course always showed a steady decline in temperature, thus proving that the temperature fell by lysis.

In almost all the patients treated with nuclein Hofbauer observed a more or less definite amount of sensibility in certain bones, which made itself apparent by the occurrence of pain on applying pressure to the part, but which disappeared at the latest within a week. This phenomenon

is probably due to a regeneration of the blood caused by the nuclein and having its seat in the bone marrow; it is also observed during the convalescent stage following malaria.

Hofbauer was able to confirm the increased excretion of uric acid following the use of nuclein or of nucleinic acid already observed by Horbaczewski, Umber, Weintraud, Kossel, Goto, Schittenhelm and Bendix, and others.

Although Hofbauer is not able to form a conclusive opinion from the results of his trials as to the value of nuclein, his cases show that the administration of nuclein displayed a favourable effect. A successful result, however, will always depend upon the use of the remedy at the earliest possible moment.

Pankow, who was induced by Hofbauer's results to adopt his method, was unable to obtain satisfactory results from the internal administration of large doses of nuclein, but following the subcutaneous injection of the remedy he observed a considerable increase in the number of leucocytes. On the other hand, Pollak's successful results in gynaecological cases speak in favour of the value of nuclein.

Owing to rapid pulse and increase in temperature consequent on laparotomy in a woman, Pollak injected subcutaneously a mixture of nuclein and sodium chloride, which was repeated daily early in the morning and in the evening. Already on the second day a typical fall in temperature occurred and coincidently a gradual decrease in the frequency of the pulse. The patient's general condition improved remarkably, and in time a cure was effected. In this case no pains in the bones were observed. In another case, too, the injections of nuclein appeared to have a beneficial effect, although the author does not venture to ascribe the cure to the action of nuclein alone. In this case, however, the pains in the bones reported by Hofbauer were observed.

If it is borne in mind that on dissolving nuclein in dilute solution of sodium hydroxide it is partly decomposed into albumin and nucleinic acid, and further that nucleinic acid, as is apparent from the following remarks, also deserves consideration as an agent for producing leucocytosis, and

Hofbauer, *Zentralblatt für Gynäkologie* 1896, Vol. 20, p. 441.

Pankow, *Beiträge zur Geburtshilfe und Gynäkologie* Vol. 9, p. 500.

Pollak, *Archiv für Gynäkologie* 1906, Vol. 79, p. 504.

in this respect is apparently even superior to nuclein, it is safe to assume that nucleinic acid, or sodium nucleinate, may be substituted for nuclein, and the latter is therefore superfluous. In addition, the use of sodium nucleinate and of its preparations, especially in the form of solutions for injections, has the advantage of greater simplicity on account of the ready solubility in water of this salt, and permits of more reliable dosage. However, it has not yet been proved that the albumin residue bound to the nucleinic acid in the nuclein molecule is entirely without any physiological or pharmacological action. Pollak feels justified in attributing to this albumin group a certain rôle in the therapeutic action displayed by nuclein, confirming Kossel's statement that "nothing justifies us in singling out one of the chemical constituents of the cell and attributing to it alone the whole problem of life".

Attempts have been made to utilise nuclein as a local dressing for wounds. C. L. Schleich found that nuclein is particularly adapted for removing necrotic material from wounds. According to his experience, it is capable of eliminating dead or dying tissue from granulating surfaces without affecting in any way the healthy vascularized parts, and therefore deserves special consideration in the treatment of wounds. In a 2 to 3 p. c. mixture with serum powder*, or in the form of an ointment, according to the statements of this author, it is capable of cleansing wounds containing necrotic or necrobiotic material to such an extent that the affected parts frequently appear as if they had been curetted. This is not only the case with dying remnants of connective tissue, such as pieces of tendons and tendon sheaths, bundles of fascia and other forms of dead tissue, but also with pathological products which display a tendency to necrobiotic decay, such as gummata and tubercles. In several cases of intractable local tuberculosis the author obtained a cure by the use of nuclein (nucleinic acid) applied in the form of a powder or ointment. As a wound stimulant it has the advantage over silver nitrate of acting only upon diseased cell material, leaving healthy tissue uninfluenced.

Schleich, *Therapeutische Monatshefte* 1894, p. 551.

* A suitable preparation for this purpose is the serum powder issued under the name of "Afermol". Compare Merck's Report 1909, p. 97.

Nucleohiston.

In an investigation of the nucleo-proteids of the thymus of calves, L. Lilienfeld obtained a nucleo-proteid by precipitating the leucocytic extract with acetic acid, and on treating this nucleo-proteid with dilute hydrochloric acid it yielded histon* and nuclein (so-called leuco-nuclein). The further study of Lilienfeld's nucleohiston by Bang, Huiskamp and Malengreau showed, however, that this product is not a uniform substance, but a mixture of a nucleo-proteid and a histon nucleinate. As it cannot be assumed that the substances obtained by these authors by different processes were identical, it is advisable to distinguish these preparations according to the method of obtaining the same, thus a nucleohiston according to Lilienfeld**, a nucleohiston according to Huiskamp, and a histon nucleinate according to Bang. The nucleohiston supplied by me corresponds approximately to Huiskamp's preparation. It is a yellowish powder, almost insoluble in water, but soluble in dilute alkalies.

Lilienfeld was of opinion that his nucleohiston represented the physiologically active component of the leucocytes, and since it splits up into nuclein, or nucleinic acid, and histon, Freund and Gross assumed that it possessed bactericidal and antitoxic properties; this assumption was confirmed to a certain extent by the results of experiments undertaken by J. G. Novy. Of course, these properties are not sufficient to effect passive immunisation against infectious diseases. It is conceivable that nucleohiston is capable of therapeutic application, in the same way as nuclein, but I have no knowledge of any references to this effect in medical

Lilienfeld, *Zeitschrift für physiologische Chemie* 1894, Vol. 18, p. 473. — Merck's Report 1896, p. 105 and 1897, p. 96.

* Histons are proteins with a basic character, therefore Huiskamp applies to nucleohiston the designation histon nucleinate.

Bang, *Beiträge zur chemischen Physiologie und Pathologie* 1903, Vol. 4, p. 115 and 331.

Huiskamp, *Zeitschrift für physiologische Chemie* 1901/02, Vol. 34, p. 32.

Malengreau, *La cellule* 1900, Vol. 17, p. 339.

** Compare Steudel, *Zeitschrift für physiologische Chemie* 1913, p. 207.

Freund-Gross, *Wiener medizinische Blätter* 1896, p. 27.

Novy, *Journal of Experimental Medicine* 1896, p. 693.

literature, nor have I received any communications on this subject from members of the medical profession.

Nucleinic Acid.

I supply the following preparations of nucleinic acid:*

Nucleinic Acid from yeast, a white or greyish-white powder** obtained from yeast nuclein; it is sparingly soluble in water, but is readily soluble in alkalies.

Animal Nucleinic Acid, a yellowish powder prepared from the thymus gland and other similar animal glands containing nuclein; it has almost the same solubility as nucleinic acid from yeast.

Sodium Nucleinate, a yellowish-white powder prepared from nucleinic acid from yeast. It is readily soluble in water and contains approximately 4.5 per cent. of sodium.

Iron Nucleinate, a light brown powder, soluble in acids, containing about 9 per cent. of iron.

Quinine Nucleinate, a yellowish-white powder, slightly soluble in water, rather more soluble in alcohol (50 per cent.) and in dilute glycerin. It contains 40 per cent. of quinine.

The physiological and pharmacological importance of nucleinic acid is on the whole identical with that of nuclein, and therefore does not call for special mention. However, attention may again be drawn to the statement by Popoff

* In addition to the salts of nucleinic acid manufactured by me, the following have been described in the literature:

b-Copper Nucleinate of Schmiedeberg, *Archiv für experimentelle Pathologie* 1907, Vol. 57, p. 309.

b-Sodium Nucleinate of Schmiedeberg, l. c. and Neumann, *Archiv für Physiologie* 1899, Supplement p. 554.

Acid b-Sodium Nucleinate of Schmiedeberg, l. c.

a-Sodium Nucleinate of Kostytshew, *Zeitschrift für physiologische Chemie* 1903, Vol. 39, p. 553.

a-Barium Nucleinate of Kostytshew, l. c.

a-Copper Nucleinate of Steudel, *Zeitschrift für physiologische Chemie* 1905, Vol. 46, p. 335.

Bismuth Nucleinate of Schmelz, *Merck's Report* 1908, p. 148.

** The anhydrous acid has a phosphorus content of approximately 9 per cent.

Popoff-Gumlich, l. c.

that nucleinic acid on internal administration is absorbed directly and passes into the blood circulation, while Gumlich found that it increases phosphoric acid metabolism. Further, reference may be made to the investigations of Parlavecchio, Tichomiroff, Vaughan and Kossel, which demonstrate that nucleinic acid precipitates the bacterial toxalbumins in the organism and renders them innocuous, produces agglutinating substances and alexines and possesses a certain amount of bactericidal power, apparent in the bacteriolytic properties exhibited by the blood after injections of nucleinic acid. According to S. Tabozzi, nucleinic acid also displays a favourable effect on the quality of the blood in general, and effects an increase in the number of red blood corpuscles and hæmoglobin content. In addition, nucleinic acid acts upon the fermentative processes in the organism as M. Tschernoruzki has shown. The most important therapeutic properties of nucleinic acid are, however, its bactericidal action and its effect of increasing the number of leucocytes.

The relation of nucleinic acid metabolism to the elimination of uric acid is dealt with in the publications on this subject by Kossel, Schittenhelm and Bendix, Kühnau, Goto, Umber, Richter and Weintraud.

Kühnau and Richter favour the view, already advanced by Horbaczewski, that the elimination of uric acid is in direct proportion to leucocytosis. Richter does not think that this connexion is a constant phenomenon. Kühnau made a careful study of the correlation between leucocytosis and uric acid elimination in artificial leucocytosis and also in the leucocytosis in different infectious diseases, and came to the following conclusions: An increase in the amount of uric acid excreted

Parlavecchio, *Archiv für klinische Chirurgie* 1909, Vol. 90, No. 1, p. 202.

Tichomiroff-Vaughan-Kossel, l. c.

Tabozzi, *Therapeutische Monatsberichte* 1904, No. 7, p. 157. —
Merck's Report 1904, p. 9.

Tschernoruzki, *Biochemische Zeitschrift* 1911, Vol. 36, p. 363.

Kossel, l. c.

Schittenhelm-Bendix, *Deutsche medizinische Wochenschrift* 1904, p. 1164.

Kühnau, *Zeitschrift für klinische Medizin* 1895, Vol. 28, No. 5.

Goto, *Zeitschrift für physiologische Chemie* 1900, p. 473.

Umber, *ibidem* 1895, Vol. 28, No. 1.

Richter, *ibidem* 1895, Vol. 27, No. 6.

Weintraud, *Berliner klinische Wochenschrift* 1895, No. 19.

occurs in a number of diseases in which leucocytosis is present. This increase is not attributable to the fever alone, as it is also present in afebrile illnesses. — A rapid decline in leucocytosis is associated with a decrease in uric acid excretion. — Experimentally produced leucocytosis shows the same behaviour; the elimination of uric acid reaches its maximum after the disappearance of the leucocytosis. — The excretion of uric acid may also be produced, in the absence of leucocytosis, by the administration of material containing leucocytes, e. g., a suspension of thymus gland. — The injection of nuclein directly causes an increase in the excretion of urates, for which the simultaneous occurrence of leucocytosis cannot be held responsible. On the other hand, the leucocytes are, if not exclusively, the principal material from which uric acid is formed.

Weintraud found that feeding with substances containing nuclein, such as thymus gland, caused a considerable increase in the formation of uric acid, and this result was confirmed by Umber. Umber established that feeding with thymus gland produced a far greater elimination of uric acid than the same amount of meat, calf's kidney or calf's brain.

Schittenhelm and Bendix studied the behaviour of nucleinic acid following its intravenous injection into rabbits. As their results do not offer any conclusions of therapeutic importance and do not permit of a brief abstract, reference should be made to the original paper*.

Of greater therapeutic importance are the results obtained by Goto. After Kossel had shown that nucleinic acid is capable of forming soluble compounds with the purin bases in the organism, Goto sought to ascertain whether uric acid exhibited the same behaviour as the purin bases. By mixing sodium urate and sodium nucleinate he obtained a solution in which uric acid was not precipitated by acids.

The results of the above mentioned authors have not been applied in the treatment of gout, at least I have been

Schittenhelm-Bendix, Deutsche medizinische Wochenschrift 1904, p. 1164.

* Compare also Ewald, Zeitschrift für experimentelle Pathologie und Therapie 1913, Vol. 12, p. 348 and Stephan, Apotheker-Zeitung 1912, No. 83, p. 816.

unable to trace any references worthy of note in the literature at my disposal.

The bactericidal action of nucleinic acid was first demonstrated experimentally by A. and H. Kossel. A. Kossel found that nucleinic acid destroyed organised albumin within a short time, and the author attributes this effect to the affinity of nucleinic acid for albuminous substances. H. Kossel then investigated the action of nucleinic acid on bacteria, and found that streptococci are killed within two hours by a 0.5 per cent. solution of nucleinic acid; staphylococci, on the other hand, proved more resistant and were killed only after six hours' contact. The positive results obtained by Wooldridge and Gramatschikoff in experimental anthrax, by Vaughan, Loewy and Richter in experimental pneumococcic infection, and by Tichomiroff in experimental streptococcic infection, are probably attributable to this property of nucleinic acid. However, the fact must not be lost sight of that it is highly probable that this bactericidal action is in large part due to the hyperleucocytosis produced by nucleinic acid. These physiological and pharmacological findings led to the therapeutic use of nucleinic acid in the following diseases.

Septic processes in surgery and gynæcology form one of the principal indications for nucleinic acid therapy. J. von Mikulicz-Radecki and H. Miyake share the honour of being the first to point to its value in these conditions. They found that injections of nucleinic acid were a valuable measure in operations on the stomach and intestines, as they increased the resistance of the peritoneum against pathogenic bacteria. According to the experience of these authors, the prophylactic use of nucleinic acid causes a considerable increase in leucocytosis and thus increases the resistance of the peritoneum about twenty times. Twelve hours before the operation they injected usually 50 c. c. of a 2 per

Wooldridge, communicated by Metschnikoff, *Virchows Archiv* Vol. 96, p. 177. — *Annales de l'institut Pasteur* 1895.

Gramatschikoff, *Annales de l'institut Pasteur* 1893, p. 812.

Vaughan, l. c.

Loewy-Richter, *Deutsche medizinische Wochenschrift* 1895, p. 240.

Tichomiroff, l. c.

Mikulicz, *Archiv für klinische Chirurgie* 1904, Vol. 73, p. 347.

Miyake, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie* 1904, Vol. 13, p. 719.

cent. (in some cases solutions of 0.5 to 4 per cent. were employed) solution of sodium nucleinate under the skin of the chest; these injections were not followed by any appreciable local or general unwelcome sequelæ, on the contrary, they exerted a favourable influence on the course of the cases treated by this procedure. Even the voiding of a considerable amount of fæces into the abdominal cavity was borne without damage. These results opened up a most promising prospect for surgery in the prevention of post-operative peritonitis.

The property of nucleinic acid of increasing the number of leucocytes and its value in infections was confirmed by the investigations of Renner, L. S. Dudgeon, A. Ross, W. Hannes, Busse, Daskalitz-Kofmann, Lassen, E. Pollak, Chantemesse, C. Stern, H. Boruttau, E. von Graff, Candela y Pla, B. Aschner, Delassus, M. Henkel, Th. Goldenberg, and others.

Busse made a special study of post-operative leucocytosis and its production by injections of sodium nucleinate. According to his observations, the injections are always followed by hyperleucocytosis; should this not take place, its absence is a bad prognostic sign. A fixed relation between the degree of leucocytosis produced and its protective action cannot, according to the author's statements, be constructed owing to the fact that the degree of hyperleucocytosis differs in various cases. The fact, established by experiment, that the

Renner, *ibidem* 1905, Vol. 15, p. 89.

Dudgeon-Ross, *American Journal of the Medical Sciences* 1906, Vol. 132, p. 569.

Hannes, *Zentralblatt für Gynäkologie* 1906, p. 681.

Busse, *Archiv für Gynäkologie* 1908, Vol. 85, p. 1.

Daskalitz-Kofmann, *Dissertation* Geneva 1907.

Lassen, *Dissertation*, Berlin 1911.

Pollak, l. c.

Chantemesse, *Bulletin de l'Académie de médecine* 1907, Vol. 57, p. 736.

Stern, *Medizinische Klinik* 1907, p. 949.

Boruttau, *Therapeutische Monatshefte* 1909, p. 305.

Aschner-Graff, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie* 1910, Vol. 22, No. 1.

Candela y Pla, *Cronica medica* (Valencia) March 10, 1910.

Delassus, *Journal des sciences médicales* 1907, No. 31.

Henkel, *Deutsche medizinische Wochenschrift* 1908, p. 1933.

Goldenberg, *Münchener medizinische Wochenschrift* 1909, p. 28.

blood withdrawn after an operation and showing a high content of leucocytes exhibits a more powerful bactericidal action on *Coli* bacilli than the blood withdrawn before the operation appears to me to be of importance, as well as the fact that animals treated with nucleinic acid show a greater resistance against bacterial infections.

On continuing his investigation of the results obtained by Mikulicz, Renner came to the conclusion that the subcutaneous injection of nucleinic acid from yeast in man first caused transient leucopenia, followed by a considerable increase in the number of leucocytes. He is of opinion that subcutaneous injection displays almost as prompt an action as intraperitoneal application, and considers the former to be more humane. Aschner, on the other hand, maintains that intraperitoneal injection is considerably more effective. Renner admits that subcutaneous injection is followed by secondary effects, these are, however, unimportant and not accompanied by any markedly unpleasant sequelæ, provided a dose of 1 gramme (15 grains) of sodium nucleinate is not appreciably exceeded. Subsequently the value of injections of nucleinic acid in laparotomies, apparent in a reduction in the mortality, was recognised by various authors, including Delassus, Faucon, de Paoli, Parlavecchio, Thirolloix and Thevenard, while von Graff questions the favourable action of nucleinic acid. He considers that the successful results recorded are in great measure due to recent advances in technique and to the greater experience of operators than to the use of nucleinic acid. This view is refuted by Paoli, who emphasises the value of injections of nucleinic acid. The results obtained by Candela y Pla are also in favour of nucleinic acid. This author has injected sodium nucleinate in a large number of cases of commencing post-operative peritonitis and reports very satisfactory results with this method*. On the whole, however, its prophylactic use will

Delassus, l. c.

Faucon, Dissertation Lille 1906.

Paoli, *Annali della facoltà di medicina di Perugia* 1909, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie* 1912, Vol. 24, p. 274.

Parlavecchio, l. c.

Thirolloix-Thevenard, *La quinzaine thérapeutique* 1907, No. 10.

* Candela y Pla at first injected a solution of 0.4 gramme (6 grains) of sodium nucleinate in 40 c. c. (1 $\frac{1}{3}$ oz) of normal saline

prove of greater service. Thus Henkel is of opinion that injections of nucleinic acid are quite capable of effecting an increase in the number of leucocytes and thereby affording protection against the invasion and dissemination of streptococci. If, however, a septic infection has manifested itself and the organism has had to fight already for some time against the micro-organisms which have entered into the blood-stream, then little or no benefit may be expected from this treatment. Therefore, in spite of Candela y Pla's favourable results, special attention must be paid to the time of giving the injection of nucleinic acid, or of performing the operation after giving an injection. The best time for performing the operation is possibly when leucocytosis is at its height, or, according to Busse, during the period of increased leucocytosis, although owing to the slow rate of decrease of hyperleucocytosis good results may still be expected after it has passed its culminating point.

Chantemesse's communications also speak in favour of nucleinic acid, and this author considers nucleinic acid to be more effective than collargol. He repeatedly observed that the severe pains following intestinal hæmorrhage in typhoid fever disappeared completely within twenty-four hours after giving an injection of nucleinic acid. It is possible, although not proved, that in these cases a small perforation of the intestine was present, which healed under the influence of the rise in the opsonic index subsequent to the injection. This was plainly evident in one case in which the administration of nucleinic acid after the appearance of peritonitis so improved the critical condition that an operation might have been performed. As this was refused the patient died; a post-mortem examination revealed the fact that through the injection of nucleinic acid the fight of the leucocytes against the infection had already been organised, and even large perforations were already blocked. Chantemesse gave as an injection 40 c.c. of normal saline solution containing 0.4 gramme of sodium nucleinate, and injected this amount subcutaneously once or twice into the region of the flank or into the outer aspect of the thigh. After a few hours pain at the

solution and then on several days injected twice daily 0.2 gramme (3 grains). Even in a case of severe hæmorrhage in typhoid with perforation he obtained by this means a striking success.

site of injection occurred, and within twenty-four hours a slight swelling and redness which disappeared on the following day; the pain was relieved by the application of opium poultices. The injection may be repeated after two or three days, and if necessary a third injection may be given; however, the dose should be decreased with each subsequent injection.

In experiments on a patient who had been treated with injections of nucleic acid for a perforation of the intestine, Chantemesse found that within twenty-four hours the opsonic index of the blood rose from 1.6 to 2.5. The stimulating phagocytic power of the patient's serum had therefore increased by almost 100 p.c., with the result that the peritoneal inflammation visibly decreased.

Hannes reports 51 cases of abdominal extirpation of the uterus (in cancer of the uterus) which were performed with the aid of injections of nucleic acid. He gained the impression that the injection of 50 c.c. of a 2 per cent. solution of sodium nucleinate ten to sixteen hours before operation assisted in overcoming slight infection, but was powerless in the presence of more severe infection. The mortality fell from 40 p.c. to 20 p.c.

The action of injections of nucleic acid of stimulating leucocytosis was confirmed by Pankow in over 90 p.c. of his cases. He studied this action in a large number of gynaecological operations and came to the conclusion that the injections are capable of creating more favourable conditions for the healing process, although a definite conclusion cannot be drawn from his collected material.

From the experiments made with nuclein, mentioned above, there is some justification for the assumption that the subcutaneous injection of nucleic acid may render valuable services in post-partum puerperal infections. Here its prophylactic use primarily deserves consideration. However, the results of trials by Pankow and von Graff do not hold out any great promise of success from nucleic acid therapy in this direction. In twelve cases Pankow failed to observe the occurrence of hyperleucocytosis; von Graff, after the injection of 40 to 50 c.c. of a 2 p.c. solution of sodium nucleinate in twelve cases, observed in five cases a rise

in temperature associated with considerable hyperleucocytosis, in three cases distinct hyperleucocytosis, in one case a rise in temperature only, and in three cases no effect whatever was observed. This result is evidence of the existence of individual sensitiveness to nucleinic acid, which throws doubt upon its efficacy as a prophylactic in special cases. According to von Graff, during the critical days in the puerperium nucleinic acid is not able to effect an absolutely satisfactory degree of leucocytosis, and its prophylactic use during birth also does not yield positive results. The valuation of artificial leucocytosis in childbirth in febrile women appears to offer special difficulties, in contradistinction to other surgical and gynaecological diseases, as is apparent from Henkel's reports. In this author's experience the appearance of the blood in puerperal fever and particularly in pyæmia differs to such an extent and is so uncontrollable that no conclusions of practical value for therapeutic treatment can be drawn.

According to C. Stern, nucleinic acid is indicated in the treatment of syphilis, principally on account of its action of increasing leucocytosis, and by its aid alone, without the use of mercury, he succeeded in causing the disappearance of luetic symptoms. For practical purposes he is in favour of combined treatment with nucleinic acid and mercury. For injection he made use of a 10 p. c. solution of sodium nucleinate, instead of the customary 1 to 2 p. c. solution, and found that it was generally well tolerated. At first he gave as an average dose 0.5 gramme ($7\frac{1}{2}$ grains) of sodium nucleinate and later increased this amount, if necessary, to 1 gramme (15 grains).

Syphilis. R. Lenzmann, who had obtained surprisingly good results with the use of quinine in syphilis, also employed nucleinic acid to intensify the quinine action by the production of hyperleucocytosis. For the sake of simplicity he prescribed quinine nucleinate in oily suspension (1 in 20 of olive oil) which can be injected intramuscularly without causing pain or local reaction. This author found that an injection of 10 c. c. of this suspension caused a considerable and lasting

von Graff, Zentralblatt für Gynäkologie 1910, No. 27, p. 900.

Stern. l. c.

Lenzmann, Deutsche medizinische Wochenschrift 1908, No. 10, p. 404. — Merck's Report 1908, p. 283.

increase of leucocytosis. Owing to the slow rate of absorption on intramuscular injection the quinine action is deficient, so that these injections have to be supplemented by the intravenous exhibition of quinine hydrochloride. Lenzmann therefore combined the intravenous injection of quinine with the intramuscular injection of quinine nucleinate in the following manner. On the first day he injected intramuscularly 0.5 gramme ($7\frac{1}{2}$ grains) of quinine nucleinate and in the evening gave an intravenous injection of 0.6 gramme (9 grains) of quinine hydrochloride; on the following day he gave 0.8 gramme (12 grains) of quinine hydrochloride; on the third day 0.5 gramme ($7\frac{1}{2}$ grains) of quinine nucleinate in the morning and 0.8 gramme (12 grains) of quinine hydrochloride in the evening; on the fifth day 0.5 gramme ($7\frac{1}{2}$ grains) of quinine nucleinate; on the sixth day 0.8 gramme (12 grains) of quinine hydrochloride; on the eighth day 0.5 gramme ($7\frac{1}{2}$ grains) of quinine nucleinate; on the ninth day 0.8 gramme (12 grains) of quinine hydrochloride; on the twelfth day 0.5 gramme ($7\frac{1}{2}$ grains) of quinine nucleinate; on the thirteenth day 0.8 gramme (12 grains) of quinine hydrochloride; on the seventeenth day 0.5 gramme ($7\frac{1}{2}$ grains) of quinine nucleinate; and on the eighteenth day 0.8 gramme (12 grains) of quinine hydrochloride. Thus within a period of eighteen days he administered 15.4 grammes (231 grains) of quinine hydrochloride and 3 grammes (45 grains) of quinine nucleinate. The value of this form of treatment was confirmed by H. Napp.

Tuberculosis. Barbier made use of injections of nucleinic acid in chronic and apyretic cases of pulmonary tuberculosis in children, giving a dose of 0.05 gramme ($\frac{3}{4}$ grain) of sodium nucleinate every second day. He made the observation that the injections gave rise to pain and local symptoms of irritation, and also produced a rise in temperature and loss of appetite. These results, which differ from previous experiences, are attributed by Chassevant to the use of nucleinic acid prepared from milt, whereas on employing nucleinic acid obtained from yeast only pain and rise in temperature are apparent. The two authors express no opinion as to the therapeutic result of this treatment. That a successful

Napp, *ibidem* 1908, No. 21, p. 919.

Barbier, *Répertoire de pharmacie* 1908, p. 232.

Chassevant, *ibidem* p. 233.

result can be obtained is clearly proved by Mougeot's and Goldenberg's observations. Mougeot injected 1 c. c. of a 5 p. c. solution of sodium nucleinate and found that this dose was well tolerated and did not give rise to any general or local reaction. In one case of pulmonary tuberculosis the effect was so satisfactory that the author proposes to undertake further trials with this method. Goldenberg injected the drug intratumorally in tuberculous abscesses, in order to produce leucocytosis, and then treated the abscesses with X rays. Already in the first case treated by this method he obtained a brilliant success. It was a case of a tuberculous abscess of the soft part in the outer aspect of the thigh, which had previously been treated without success for a long time with injections of iodoform, and which healed under the use of this combined treatment. The cosmetic result also was highly satisfactory, as the healed part could in no way be distinguished from the healthy skin.

Apart from the production of hyperleucocytosis, an explanation of the action of nucleinic acid in tuberculosis may be found in the results of experiments by R. Bachrach and J. Bartel. These authors found that free nucleinic acid does not inhibit the virulence of tubercle bacilli in vitro for some time, but it is destroyed if albuminous substances are also present.

Paralytic Dementia. The observation is often made that cases of paralytic dementia (progressive paralysis) in which the diagnosis has been established with certainty spontaneously show remissions and recover, or this occurs after fever and suppurative processes. Hitherto no satisfactory explanation had been forthcoming, until O. Fischer sought an explanation in the hyperleucocytosis which always accompanies suppuration, and his experiments justify this conclusion. He succeeded in causing an increased and lasting leucocytosis by means of a sufficient number of injections of sodium nucleinate (up to 32 injections). This treatment caused at first an increase in the swelling of the limb, which, however, subsided gradually on continuing the treatment and was not followed by any undesirable sequelæ. He obtained the

Mougeot, *Journal des praticiens* 1904, No. 31.

Bachrach-Bartel, *Wiener klinische Wochenschrift* 1907, No. 35, p. 1040.

Fischer, *Prager medizinische Wochenschrift* 1909, No. 29, p. 401.

following results: In four patients a general remission took place, two of whom — expansive forms of disease — became calmer and were discharged psychically cured. According to the statements of the author, one of these patients remained for almost two years in a slightly maniac state under home treatment; the other was able to resume his occupation for nine months after undergoing this treatment, and he behaved in a perfectly correct manner, with this difference that he was unable to count as well as formerly. Of the other two patients — simple forms of dementia — the one came under treatment in a very advanced stage of imbecility. He showed a considerable improvement, but after four weeks his condition became worse. The fourth case improved both from a somatic as well as psychic point of view. Four patients died and fourteen exhibited no appreciable improvement in their condition. In twenty-two control patients not treated with nucleinic acid no remission was apparent and up to the time of publishing his paper the author reports eight deaths.

Although the number of cases treated by Fischer was not so great as to permit a definite conclusion regarding the value of nucleinic acid treatment in paralytic dementia, yet the total result may be regarded as favourable. In this connexion it may be mentioned that J. Donath obtained very satisfactory results in patients in the initial stage of paralysis.

Donath employed a 2 p.c. solution of sodium nucleinate in a 2 p.c. sterile solution of sodium chloride. 50 to 100 c.c. of this solution were injected subcutaneously with aseptic precautions at intervals of five to seven days, a fresh site being chosen for each injection. The injections were followed by a rise in temperature up to 38.5° C., on an average. To distinguish this rise in temperature from that due to febrile symptoms Donath termed it "hyperthermia". They also produced an increase in the number of leucocytes up to 61,000. In all the author gave about eight injections. According to his statements, this pyretic treatment is designed to destroy the poisonous metabolic products of the disease through the action of the hyperthermia and the hyperleucocytosis and the

Donath, Wiener klinische Wochenschrift 1909, p. 1289. — Allgemeine Zeitschrift für Psychiatrie und psychisch-gerichtliche Medizin 1910, No. 3. — Psychiatrisch-neurologische Wochenschrift 1910, No. 15. — Berliner klinische Wochenschrift 1910, p. 2343 and 1911, p. 555.

resulting increased oxidation. It is especially indicated when antiluetic treatment is no longer advisable. This treatment will, however, frequently prove useful in cases in which syphilitic infection has been present, but has not been satisfactorily treated with mercury. The improvement is particularly apparent in the disappearance of the tremor and the excitement, and in the ability of the patients to count better and speak more plainly; the memory also shows an improvement.

Donath treated twenty-one cases by his method and in ten obtained an appreciable improvement, that is to say the patients were so far restored to health as to become once more capable of earning their own living; in five cases an objective and subjective improvement followed without leading to a restoration of the patients' former abilities, and in six cases no success was obtained. Donath has not observed any injurious secondary effects referable to his method.

The reports of Klieneberger and Loewenstein are less favourable. In fifteen cases of paralytic dementia Klieneberger was unable to observe any appreciable improvement following the use of injections of nucleinic acid, although during institutional treatment some of the patients showed a considerable increase in weight. In some patients the injections were followed by acute, but transient, aggravation of their condition. The injections were not well borne and gave rise to painful infiltrations at the site of injection. Loewenstein also was unable to obtain any noteworthy successes (in thirteen cases). He is of opinion that the use of nucleinic acid does not lead to any greater improvement than is the case even without the use of special treatment.

The failures reported by Klieneberger are in Donath's opinion due to fact that in most cases patients in an already advanced state of paralysis were submitted to his method of treatment, whereas he laid stress upon the fact that nucleinic acid is capable of proving useful only in the initial stage of paralysis. Infiltrations, he states, may be avoided by changing the site of injection. Three of his patients whom he has kept under strict observation are still attending to their occupations, one of these for the past three years, although before being treated by nucleinic acid

he had been completely incapacitated in consequence of advanced dementia. In ten other cases under treatment Fischer also observed an improvement in five, of which three have since resumed their occupations. In ten control cases he observed an improvement only once, and that after prolonged suppuration.

Jurmann tried the use of nucleinic acid in seventeen paralytics and obtained satisfactory results in seven cases, so that he recommends the further use and trial of this method.

Hussels among five cases observed a noteworthy positive result in one instance only, in a rather advanced case, but in the other cases no success worthy of mention was obtained.

Based on the results of his experiments, C. Tsiminakis comes to the conclusion that the use of nucleinic acid in the treatment of paralysis should not be discarded, on the contrary, it should be taken into consideration as apart from treatment with tuberculin or killed cultures of staphylococci and streptococci we are almost powerless to combat this disease. Although nucleinic acid is not able to arrest the mental decay in every case, yet the results obtained by Tsiminakis show remissions and an improvement in many instances, and therefore speak in favour of the value of nucleinic acid treatment. His patients, all of whom showed a positive Wassermann reaction, were first given three injections of salvarsan, an injection of 0.3 gramme at intervals of eight days. Twenty days after the last injection of salvarsan he began treatment with nucleinic acid, giving eight injections at intervals of seven days and using a 2 p.c. solution of sodium nucleinate in a 2 p.c. solution of sodium chloride*.

Becker is also in favour of the use of sodium nucleinate in paralysis. According to his report it has the advantage

Fischer, Prager medizinische Wochenschrift 1911, No. 8 and 1913, No. 2.

Jurmann, Russkij Wratsch 1911, No. 46.

Hussels, Archiv für Psychiatrie 1911, Vol. 48, No. 3, p. 1113.

Tsiminakis, Wiener klinische Wochenschrift 1912, No. 49, p. 1939.

* Details of the dosage are not given in the original communication.

Becker, Klinisch-therapeutische Wochenschrift 1913, No. 21, p. 635.

over salvarsan of being harmless and can be employed by any practitioner. He does not share the pessimistic view of some authors (mentioned above). He has repeatedly injected sodium nucleinate and is convinced of its comparative harmlessness. However, he draws attention to one drawback which has not received sufficient mention in the literature, and this is the frequently occurring insufficient absorption of the injected solution. In spite of aseptic precautions a fluctuating sac may form which takes about a week to disappear and sometimes suppurates. Suppuration in paralysis is not an undesirable symptom, since it is known to beneficially influence remissions. In adopting nucleinic acid treatment for the first time the practitioner must be prepared for this emergency, and also to hear complaints of pain caused by the injections, especially from weak-minded paralytics. Further, according to Becker, the use of nucleinic acid should not be suspended at once on the appearance of an improvement.

A. Moretti endorses the opinions of Tsiminakis and Becker regarding the value of sodium nucleinate in paralytic dementia and in dementia præcox. Although he records a number of failures, the author observed the mental symptoms to disappear in three cases of dementia præcox after repeated injections of this drug. He is fully aware of the inconclusiveness of these results, but urges that trials with nucleinic acid should be made in a disease the etiology and pathogenesis of which are as yet unknown and for which there is at present no causal treatment. Especially in the initial stage of the malady a trial with the drug is recommended.

At the Psychiatric Congress held in Kiel, Meyer stated that combined treatment with nucleinic acid and salvarsan might under certain circumstances hold out a promise of success.

H. Lundvall made use of a combination of nucleinic acid, arsenic and sodium cinnamate to stimulate leucocytosis in dementia præcox. He prescribed it in the following form:

Sod. nuclein.	100 grammes ($3\frac{1}{3}$ oz)
Acid. arsen.	0.2 gramme (3 grains)
Hetol	4 grammes (60 grains)
Aq. destill.	400 grammes ($13\frac{1}{3}$ oz)

Moretti, Rassegna di studi psichiatrici 1913, Vol. 3, p. 269.

Meyer, Archiv für Psychiatrie 1912, No. 1.

Lundvall, Sonderbroschüre, Kristiania 1912, Nationaltrykkeriet.

Later he employed the following solution:

Sod. nuclein.	100	grammes	(3 $\frac{1}{3}$ oz)
Acid. arsen.	0.05	gramme	($\frac{3}{4}$ grain)
Hetol	10	grammes	(150 grains)
Aq. destill.	400	„	(13 $\frac{1}{3}$ oz)

The solution is filtered and sterilized. According to the action obtained by the use of this solution 2 to 15 c.c. (34—255 min.) are injected subcutaneously. A more or less painful infiltration is formed at the site of injection and is treated by applying moist compresses. The author has never observed the formation of an abscess. On the other hand, a few hours after the injection a considerable rise in temperature occurs, often accompanied by rigor and discomfort, which usually subsides within a short time; parallel with it there is an increase in leucocytosis. Of twelve cases treated by this method two were cured, five improved greatly and two showed a slight improvement. Three cases in which the diagnosis of dementia præcox was uncertain showed no improvement.

A communication by Tschernoruzki may be adduced in explanation of the action of nucleinic acid in paralysis. He found that the intravenous injection of nucleinic acid into the brain of animals causes an increase in ferments such as diastase, amylase and protease.

Multiple Sclerosis. S. Bondi reports remarkable successes in this affection. His trials extended to eleven cases. In eight cases injections of nucleinic acid produced a striking improvement, in three cases the patients did not return for further treatment and therefore the effect of nucleinic acid could not be controlled; in one case only no improvement was observed after seven injections.

Rickets. Out of a large number of remedies employed by P. Sittler in the treatment of rickets nucleinic acid proved the most useful, as it exerted a favourable influence on the rachitic osseous process. He prescribed a mixture of sodium nucleinate and calcium glycerophosphate in powder or tablet form. According to the age of the child, sodium

Tschernoruzki, *Biochemische Zeitschrift* 1911, Vol. 36, p. 363.

Bondi, *Münchener medizinische Wochenschrift* 1911, p. 2644.

Sittler, *Münchener medizinische Wochenschrift* 1907, No. 29, p. 1435.

nucleinate was given internally in daily doses of 0.2 to 0.5 gramme (3—7½ grains), and 0.1 to 0.25 gramme (1½—4 grains) of calcium glycerophosphate. The subcutaneous exhibition of nucleinic acid should also prove useful, as is apparent from a report by J. Meisen. In this author's experience the administration of nucleinic acid always causes hyperleucocytosis without any accompanying injurious by-effects — it deviates the neutrophile blood picture to the left in Arneth's sense, i. e., an increase in the mononuclear neutrophiles does not take place. Repeated injections of nucleinic acid effect an increase and decrease in the number of red blood corpuscles and in the hæmoglobin content and strengthen the bones in the course of development.

Cirrhosis of the Liver. P. Mezernitzky reports on this subject. According to his communications, doses of 5 to 15 grammes (75—225 grains) of sodium nucleinate display a powerful diuretic effect in cirrhosis of the liver and in ascites, which rapidly causes the disappearance of the ascites.

Psychoses. The action of injections of nucleinic acid of increasing the ferments in the brain, studied by Tschernoruzki, is an incentive to try the effect of nucleinic acid in psychiatry as well as in paralysis. To my knowledge the only communications bearing on this subject are by J. Lépine, and were published prior to those of Tschernoruzki; they do not refer to alterations in the fermentative processes induced by the action of nucleinic acid but to its property of stimulating leucocytosis. At the occasion of the publication of the results obtained by Fischer and Donath this author drew attention to the fact that already in 1907 he had made experiments with nucleinic acid in cases of mental disease. At the same time he states that his trials in seventeen cases of general paralysis were not so satisfactory as were the results obtained by the above mentioned authors in paralytic dementia.

For injection in various psychoses he made use of a 1 p.c. solution, of which he injected 50 c.c.; later, in order to avoid injecting such large amounts of fluid, he employed

Meisen, *Medizinische Klinik* 1911, p. 1946.

Mezernitzky, *Münchener medizinische Wochenschrift* 1910, No. 19, p. 1032.

Lépine, *Presse médicale* 1910, No. 9, p. 65. — *Lyon médical* 1907, Vol. 109, p. 788.

2 and 5 p.c. solutions of which amounts corresponding to 0.4–0.5 gramme (6–7½ grains) of sodium nucleinate were injected. According to the nature of the case the injections were frequently repeated at intervals of a few days. Special care must be taken to ensure sterility of the solution, as very probably the intensity of the by-effects, such as infiltrations and pain at the site of injection, is more or less dependent upon this factor. As the sterilisation of solutions of sodium nucleinate demands great care and experience owing to the readiness with which the drug decomposes, the employment of a reliable preparation issued ready for use in ampoules is to be preferred, such as are supplied by me.

From the results reported by Lépine the conclusion may be drawn that nucleinic acid treatment is capable of rendering good service in mental confusion and in maniac depression; in the delirium of degenerates the results are variable, while they are unsatisfactory in dementia præcox, conditions of fear in the insane, epilepsy, general paralysis and persecution mania.

Scarlet Fever and Erysipelas. According to M. G. Moliakow, nucleinic acid treatment deserves special consideration in scarlet fever and erysipelas. He has studied the action of the drug in 90 cases, and obtained good results, particularly in the initial stages of the affection. If the injections were begun already on the second day of illness all the symptoms rapidly subsided and this was accompanied by a fall in temperature, whereas the result was less conspicuous in patients in whom treatment had been begun on the third to sixth day of illness, but even in these the favourable influence of the drug was apparent. Compared with other methods the mortality also decreased. Moliakow prescribed 0.1 gramme (1½ grains) of sodium nucleinate for each year of the child's life, so that a child of ten years was given a dose of 1 gramme (15 grains). As by-effects he observed pain at the site of injection, and in several cases headache, but no infiltrations occurred.

In chronic urticaria, Weill, Gardère and Goyet made use of injections of nucleinic acid in one case, that

Moliakow, *Russkij Wratsch* 1912, No. 9, p. 301.

Weill-Gardère-Goyet, *Lyon médical* 1912, p. 100. — *Therapeutische Monatshefte* 1913, p. 84.

of a girl, aged eleven, who had been unsuccessfully treated by the usual remedies. An injection of 0.5 gramme ($7\frac{1}{2}$ grains) of sodium nucleinate in 10 c.c. ($\frac{1}{3}$ oz) of normal saline solution was given subcutaneously with the result that the urticarial eruptions remained absent for seventeen days, probably in consequence of the leucocytosis produced and which persisted for several days.

In acute articular rheumatism, too, according to Moliakow, nucleinic acid is serviceable, as he was able to observe a remission in the pain after an injection of 1 gramme (15 grains) of sodium nucleinate. His experiments with the drug in typhoid fever, on the other hand, were not followed by any noticeable success*, as was also the case in dothienenteritis.

E. B. Blumenau also reports upon the value of sodium nucleinate in erysipelas. His communications are particularly valuable for the fact that his trials extend to 77 women in whom the affection was present in a severe form and was accompanied by pronounced toxic symptoms, irritation of the membranes of the brain, severe headache, pains all over the body, nausea and rapid pulse. Intramuscular injection (into the buttocks) is, according to the author, preferable to subcutaneous injection. Before injecting, the site of injection was disinfected with alcohol and ether, and after the injection with tincture of iodine, and by this precaution complications were avoided. At first only 1 gramme (17 min.) of a 10 p.c. solution of sodium nucleinate was injected, in obstinate cases this dose was then increased to 2—3 grammes (34—50 min.). The injections were repeated every second or third day, on days showing various temperatures in order to exclude the possibility of the treatment coinciding with the natural improvement in the affection. The beneficial effect of this treatment was apparent by the fact that in about half his cases the crisis occurred already after a single injection. The best results may be expected from the early use of nucleinic acid, e. g., on the second day

* Kukowerow and Zorokowitsch were also unable to observe any action after injections of nucleinic acid in typhoid fever. *Semaine médicale* 1913, No. 17, p. 195.

Blumenau, *Wratschebnaja Gazeta* 1911, No. 45.

Sicard-Gutmann, *Bulletin et mémoires de la société médicale des hôpitaux de Paris* 1912, Vol. 28, p. 171.

of the appearance of the affection. In septic erysipelas, however, this treatment is ineffective.

Hæmophilia. In two cases of acquired hæmophilia which had persisted for 12 and 14 years, Sicard and Gutmann obtained a complete success with the use of injections of nucleinic acid, and this result should draw attention to its employment in this and other similar affections. In view of the harmlessness of nucleinic acid a trial with it can be made even in cases where the diagnosis between hæmophilia and purpura is doubtful. The authors gave intramuscular injections of 0.15 gramme ($2\frac{1}{3}$ grains) of sodium nucleinate in 15 p.c. aqueous solution at intervals of four to five days and obtained a cure by this means.

Treatment of Wounds. As nuclein has proved itself a good remedy in the treatment of wounds (compare above), a beneficial effect on wounds may also be expected from the application of nucleinic acid. H. J. Achard has made experiments in this direction, based upon the antitoxic action of nucleinic acid and its property of stimulating leucocytosis. After cleansing the wound with sterile water he applied gauze compresses soaked in an aqueous solution of sodium nucleinate, or the wound was irrigated with the solution and then covered with an aseptic dressing. The results obtained were without exception satisfactory.

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Preparations Used for Radiographic Examinations.

When Röntgen in 1895 discovered his X-rays, the importance of this epoch-making discovery was fully appreciated by the theorist, but few foresaw that the practical utilisation of X-rays in medicine was to become an accomplished fact within so short a time. There can be no doubt that up to the present medical science deserves the credit of having put Röntgen's discovery to the greatest practical use, and to-day no hospital or clinic is able to do without skiagraphy, Röntgenology, radiography, or whatever other name may be applied to this new branch of medicine. The practical application of X-rays in surgery was followed by brilliant results, and soon attempts were made to utilise the properties of Röntgen rays in other branches of medicine. The possibility of exactly locating the position of a foreign body in the organism by the shadow seen on the photographic plate after radiographic examination, suggested a method of diagnosis based upon the opacity of certain substances to X-rays. By filling cavities of the body with a material which is more or less opaque to X-rays a shadow is cast on the photographic plate, which shows the position and form of the cavity, and from its appearance the normal or abnormal condition of the cavity can be diagnosed.

This method of diagnosis has been found particularly useful in the examination of gastro-intestinal conditions. For this object it was necessary to find a substance which is opaque to X-rays and which, administered orally or rectally, completely fills the stomach or intestine. In the first place, the substance used for this purpose must be entirely devoid of any injurious effect upon the organism, or, and this practically amounts to the same, it must be insoluble so as to exclude absorption. Another requirement is that the material employed shall be free from any injurious substances. In the following notes a brief description is given of the substances which have been tried and are used for radiographic examinations.

Barium Sulphate.

At the present day, barium sulphate (BaSO_4) is undoubtedly the most used preparation for radiographic examina-

tions, since it not only complies with the requirements enumerated above, but is also the cheapest available substance. Its use for this purpose was suggested by P. Krause. In making use of this substance the fact must not be forgotten that technical products are on the market, which, in addition to barium sulphate, also contain barium phosphate, barium nitrate, and barium carbonate, and as these salts are soluble and extremely poisonous, it follows that great care must be taken to avoid using a preparation containing any of the latter. Administered internally, barium sulphate is practically insoluble, whereas barium phosphate and barium nitrate readily dissolve already in the fluid in which they are administered (barium meal). Barium carbonate is dissolved in the acid gastric juice. The cases of poisoning reported in the literature* were due to the presence of these soluble salts of barium. Another point of great importance in prescribing barium sulphate is the avoidance of any abbreviations likely to cause confusion. For instance, cases are known where instead of barium sulphate barium sulphide, which is soluble, has been prescribed or demanded**. For this reason the prescriber is urged to write out in full "Barium sulphate for internal use for X-ray examinations". The pharmacist then knows that a special quality of barium sulphate is to be dispensed, which must comply with the following requirements:

Barium sulphate extra pure is a fine white powder, almost insoluble in water and in dilute acids. — If 1 gramme of barium sulphate be added to a solution of 5 grammes of crystalline sodium carbonate in 15 c. c. of water and boiled for one minute, the liquid, after being filtered and acidulated with hydrochloric acid, should yield a white precipitate with solution of barium chloride. The residue left on the filter, after washing with water, is partly soluble in nitric acid, and the solution thus obtained also yields a white precipitate with dilute sulphuric acid. — 10 grammes of barium sulphate are heated to boiling with 10 c. c. of acetic acid (sp. gr. 1.064) and 90 c. c. of water, and filtered. 50 c. c. of the filtrate are evaporated to dryness on a water-bath, the residue treated with 20 c. c. of water and the solution filtered. (The first filtrate obtained after boiling with the dilute acetic acid should

* Compare *Pharmazeutische Zeitung* 1912, p. 482.

** Compare *Pharmazeutische Zeitung* 1912, p. 454.

not be used as such in testing for barium). If a few drops of dilute sulphuric acid be added to the filtrate, no precipitate of barium sulphate should form in the course of an hour. (The presence of barium carbonate and soluble salts of barium may be detected by this test). — 25 c.c. of the acetic acid extract should not be affected by hydrogen sulphide solution (absence of heavy metals). — If 2 grammes of barium sulphate and 10 c.c. of nitric acid (sp. gr. 1.149—1.152) be heated to boiling and filtered, the filtrate, after the addition of solution of ammonium molybdate, should not yield a yellow precipitate within the course of an hour (absence of barium phosphate). — A mixture of 2 grammes of barium sulphate with 10 c.c. of stannous chloride solution should not assume a dark colour in the course of an hour.

The preparation I supply under the designation of "Barium Sulphate Extra Pure, Free from Phosphate and Nitrate, for Radiographic Examinations" complies with the above mentioned requirements.

The suggestion has been made to apply a coined name to preparations of this kind, such as "skiabaryt"*, in order to avoid errors. Although I was the first to supply a pure quality of barium sulphate answering all requirements for radiographic work, I have abstained from issuing it under a special name, since barium sulphate is so old and well known a substance and can be prepared by any manufacturer or pharmacist, who would be at liberty to call his own brand by any fancy name. This would lead to even worse confusion and would also compel the pharmacist to stock the various brands prescribed by doctors, and the former would have to assume full responsibility for the purity of each preparation. Under the circumstances he is able to order a suitable preparation of barium sulphate in bulk, assure himself of its purity by analysis and dispense it in the amounts prescribed. He is thus able to comply with the regulations, and the doctor may safely make use of the preparation he has ordered.

C. Bachem was the first to undertake the pharmacological investigation of barium sulphate, and he established that it caused no harm during its passage through the gastro-intestinal tract. Günther thereupon tested the substance in

* Skiabaryt from *σκιά* = shadow and the word *Baryt* (barium oxide). Bachem-Günther, Deutsche medizinische Wochenschrift 1911, No. 15, p. 717.

practice, at first in small doses and later in amounts of 100 to 150 grammes. In 60 persons to whom barium sulphate was administered these large amounts caused no injurious effect whatever. Günther lays stress on the fact that only an absolutely pure preparation should be used. In the thousands of cases in which it has since been used this substance has fully fulfilled its purpose, and up to the present no instance has been reported in which the use of pure barium sulphate has been attended by any unwelcome sequelæ. Up to the present no proof has been adduced showing that barium sulphate is altered by any substance present in the stomach or intestine, and by which it might be converted into a soluble compound, quite apart from the fact that an action of this kind would be contrary to the chemical properties of barium sulphate. The insolubility of barium sulphate is a special advantage it possesses over bismuth carbonate and bismuth subnitrate, which are both extensively used for the same purpose. Certainly, in cases in which the medicinal action of those bismuth compounds which are partly soluble in the gastric juice is to be avoided, the absolute freedom from medicinal action possessed by barium sulphate would make its use appear preferable to that of the former for radiographic examinations. This is the case, for instance, in examinations of the motility of the stomach, in which F. Best and O. Cohnheim found that the evacuation of the stomach was delayed by one hour by bismuth subnitrate, whereas barium sulphate had no effect upon the duration of evacuation.

The innocuousness of barium sulphate is further definitely established by the investigations of Nieden, Groedel and Levi, Schwarz, Bensaude and Ronneaux,

Best-Cohnheim, Münchener medizinische Wochenschrift 1911, No. 51, p. 2732.

Nieden, Deutsche medizinische Wochenschrift 1911, No. 33, p. 1515.
Groedel-Levi, Fortschritte auf dem Gebiet der Röntgenstrahlen Vol. 17, p. 55.

Schwarz, Wiener medizinische Wochenschrift 1912, No. 16. —
Berliner klinische Wochenschrift 1912, No. 16, p. 726, No. 30, p. 1424.

Bensaude - Ronneaux, Presse médicale 1911, p. 520. — Merck's Report 1911, p. 170.

Holst and Schlesinger, Peyer, Faulhaber and E. Stierlin.

Barium sulphate is administered in the form of a meal or soup, and most hospitals and clinics have their own special formulas. The preference is given to a meal prepared with cornflour. Günther prescribed for examinations of the stomach and intestine a mixture containing 20 p. c. of barium sulphate, so-called barium meal. It is prepared by boiling a mixture of: 150 grammes (5 oz) of barium sulphate, 15 grammes ($\frac{1}{2}$ oz) of cornflour, 15 grammes ($\frac{1}{2}$ oz) of sugar, 20 grammes ($\frac{3}{4}$ oz) of cocoa and 500 grammes (17 oz) of water. The author employs a meal containing 40 p. c. of barium sulphate for examinations of the œsophagus and for diagnostic examinations of the stomach. As barium sulphate is absolutely tasteless it has no effect upon the palatability of this mixture. For the diagnosis of stenosis of the small intestine and of ileus of the small intestine, Stierlin employed a meal consisting of 80 grammes ($2\frac{2}{3}$ oz) of barium sulphate and 200 grammes (7 oz) of boiled semolina. For rectal injection, which is especially adopted in examination of the large intestine, Faulhaber recommends the following formula: 30 grammes (1 oz) of cornflour are boiled with $\frac{3}{4}$ to 1 litre (25 to 33 oz) of water to form a thin paste, to which is added a suspension of 200 grammes (7 oz) of barium sulphate in 500 c. c. (17 oz) of water. On the day before the examination a laxative (compound powder of liquorice, etc.) is administered, and immediately before the

Holst - Schlesinger, Münchener medizinische Wochenschrift 1912, No. 6, p. 312.

Peyer, Zeitschrift für Röntgenkunde 1912, Vol. 14, p. 41.

Faulhaber, Münchener medizinische Wochenschrift 1913, No. 17, p. 916. In his monograph "Die Röntgendiagnostik der Magenkrankheiten", 1912, the author warned against the use of barium sulphate as he had frequently observed nausea lasting several hours after its use. However, the author had used pure barium sulphate instead of "Barium Sulphate Extra Pure, for X-Ray Diagnosis". Since using the preparation issued by me and specially manufactured for radiographic examinations he has never observed even the slightest unwelcome secondary effects. In his experience 100 grammes ($3\frac{1}{3}$ oz) are quite sufficient for an examination of the stomach.

Stierlin, Medizinische Klinik 1913, p. 983.

Faulhaber, Sammlung zwangloser Abhandlungen aus dem Gebiete der Verdauungs- und Stoffwechsel-Krankheiten 1913, Vol. 5, No. 1.

examination the bowel is emptied with an enema. The injection is performed with an ordinary douche can and a short rectal tube; the patient is first made to lie on his left side and then on his stomach.

Pure barium sulphate is undoubtedly preferable* to other substances for radiographic examinations on the following grounds: the pure substance is innocuous and its use free from danger, while its purity can easily be established by analysis; it is colourless, that is, white, and tasteless and can be administered in a meal in a palatable form; it saves time as the single examinations can follow at shorter intervals than is the case when using bismuth compounds, owing to its property of stimulating digestive activity, and lastly for the reason that it gives good shadows of the small intestine, thereby facilitating examinations**.

Bismuth Carbonate.

Bismuth carbonate is a fine white powder of varying composition; it should yield not less than 90 p. c. bismuth oxide (Bi_2O_3). It is insoluble in water, but soluble in acids.

After the first cases of poisoning caused by the use of bismuth subnitrate became known, it was assumed that the nitrate component of bismuth subnitrate was responsible for its harmful effect, since the toxic symptoms revealed themselves primarily in the form of methæmoglobinæmia, and at the recommendation of Groedel and E. Meyer bismuth carbonate was used as a substitute. Administered per os, it is scarcely if at all decomposed by the acid gastric juices, this is due to the fact, in the authors' opinion, that the swollen starch-containing vehicles protect it from being acted upon by the gastric acid. Meyer administered 20 to 30 grammes ($\frac{2}{3}$ —1 oz) of bismuth carbonate alone, or mixed with kaolin, in suspension in water or milk. Groedel questions the advisability of adding kaolin, as he fears that many patients may object to take a meal containing kaolin. On the other hand, the addition of kaolin is said to have proved beneficial in rectal injections.

* Compare Faulhaber, l. c.

** Compare Groedel, Archives of the Röntgen Ray 1913, Vol. 17, p. 420.

Groedel, Wiener klinische Rundschau 1908, p. 273.

Meyer, Therapeutische Monatshefte 1908, p. 388.

Kaestle, Albers - Schönberg, Bensaude and Rivet, Hayem, Levy-Dorn and M. Haudeck were among the first to express themselves in favour of the use of bismuth carbonate. Haudeck and Groedel have used it in thousands of cases without any ill effects. However, this was also the case with bismuth subnitrate, and cannot be adduced as a proof of the absolute innocuousness of bismuth carbonate. Lipowski observed transient cyanosis and small pulse after the administration of 30 grammes (1 oz) of bismuth carbonate to a young girl, and L. Metzger, after a dose of 40 grammes ($1\frac{1}{3}$ oz) of bismuth carbonate given in semolina paste, observed the occurrence after 30 hours of pains and tenesmus in the region of the rectum, which disappeared after giving enemata. He is of opinion that the use of such large doses of bismuth carbonate is only justifiable if there is a possibility, if necessary, of rapidly removing the substance by enemata. W. Alexander states that a severe case of bismuth poisoning was reported at the fifth Röntgen Congress. Therefore, such instances are not altogether excluded in using bismuth carbonate.

L. Lewin, amongst others, deals with the question as to whether the toxic symptoms following the use of bismuth subnitrate are attributable to the bismuth or nitric acid component of this substance. He is of opinion that all the intoxications are due to bismuth poisoning, and this view finds a certain support in the fact that up to the present toxic symptoms have very rarely been observed to follow the use of bismuth carbonate. Other observers, such as Bensaude and Rivet, attribute these symptoms to nitrite poisoning. C. Kaestle, in oppo-

Albers-Schönberg, Deutsche medizinische Wochenschrift 1909, No. 20, p. 878.

Bensaude-Rivet, l. c.

Hayem, Münchener medizinische Wochenschrift 1909, p. 1053.

Levy-Dorn, Münchener medizinische Wochenschrift 1909, p. 942.

Haudeck, Verhandlungen des Kongresses der deutschen Röntgen-gesellschaft in Berlin. April 1910.

Lipowsky, Münchener medizinische Wochenschrift 1909, p. 942.

Metzger, Medizinische Klinik 1911, p. 881.

Alexander, Deutsche medizinische Wochenschrift 1909, p. 878.
(Anmerkung.)

Lewin, Münchener medizinische Wochenschrift 1909, No. 13, p. 643.

Kaestle, Münchener medizinische Wochenschrift 1909, No. 18, p. 919.

sition to Lewin, also maintains that the cases of methæmoglobinæmia hitherto observed are due to nitrite poisoning. According to a communication by O. Schumm and A. Lorey, toxic symptoms may be caused by both constituents — bismuth as well as nitrite. According to Kaestle, the occurrence of toxic symptoms after the use of bismuth salts which are insoluble in water depends upon the capacity of the organism to dissolve a certain proportion of the compound, with the result that it is absorbed. For this reason the possibility of toxic symptoms supervening after the administration of large doses of bismuth carbonate must be reckoned with. It is still open to doubt whether this fact justifies one in warning against the use of bismuth carbonate. Possibly the method recommended by V. Schmieden and F. Härtel is the best means of avoiding the occurrence of toxic symptoms. These authors are among those who have never observed the occurrence of unwelcome effects following the use of bismuth subnitrate, and have adopted the use of bismuth carbonate only as a result of the statements made by Meyer and Kaestle to the effect that caution is necessary when using the former for diagnostic purposes. Even with the use of bismuth carbonate these authors try to exclude any possibility of toxic symptoms by washing out the stomach as soon as practicable after the examination.

Haecker, who formerly always employed a mixture of bismuth subnitrate and kaolin and sometimes observed toxic symptoms such as vomiting, headache, irregular pulse and cyanosis, never observed any unwelcome secondary effects to follow the use of bismuth carbonate. He injects by means of a stomach tube a mixture of 30 grammes (1 oz) of bismuth carbonate and 200 grammes (7 oz) of kaolin in 400 c. c. (14 oz) of water, and the examination is made with the patient lying on his stomach. This method is said to yield excellent results especially in the diagnosis of pathological changes of the stomach.

For special purposes the use of gelatin capsules filled with bismuth preparations has been recommended. Thus, G.

Schumm-Lorey, *Medizinische-kritische Blätter Hamburg* 1910, p. 76.
Schmieden-Härtel, *Berliner klinische Wochenschrift* 1909, No. 15, p. 669; No. 16, p. 721 and No. 17, p. 772.

Haecker, *Münchener medizinische Wochenschrift* 1910, No. 16, p. 884.

Holz-knecht and K. Fujinami have employed Kaestle's bismuth capsules with good results for determining the "gross motility" of the stomach. These capsules are made of formalised gelatin and are filled with a bismuth preparation; they are prepared in two varieties, the one containing air and the other not containing any air, the former sink in water and the latter float upon water. One of each kind is administered to the patient with a suitable amount of water and the examination then performed. A control is made every twenty minutes, and in this way the rate of evacuation of the stomach may be determined by the time taken by the two capsules to reach the bottom of the stomach.

In order to satisfy the most stringent requirements I supply for Roentgenological examinations a specially prepared bismuth carbonate which is absolutely free from any traces of nitric acid, i. e., bismuth subnitrate. It is issued under the designation of "Bismuth Carbonate Extra Pure, Free from Acid, for X-ray Examinations".

Bismuth Subnitrate.

The official salt consists of a mixture of basic nitrates, very probably $\text{BiONO}_3(\text{OH})_2$ and $\text{BiONO}_3 \cdot \text{BiO} \cdot \text{OH}$. It is a white powder, yielding 80 to 81 p. c. Bi_2O_3 . It is insoluble in water; its solubility in acids depends upon the concentration of the latter.

Pharmacologically bismuth subnitrate is considered to be a harmless drug, and for this reason may be administered in large single doses, up to 20 grammes ($\frac{2}{3}$ oz). This assumption is based upon the fact that although traces may be dissolved by the acid gastric juices, in the intestine it is converted into insoluble bismuth sulphide, which is not taken up by the intestinal epithelium, consequently the drug is not absorbed and is excreted with the fæces. If, therefore, the internal administration of bismuth salts is followed by toxic symptoms such as nephritis, stomatitis, diarrhoea, vomiting, etc., this is assumed to be due to a lesion of the intestinal epithelium. The use of bismuth subnitrate, therefore, does not exclude the possibility of toxic symptoms supervening, although it must be conceded that most of the instances of bismuth or

nitrite poisoning reported in the literature followed the external application of the preparation. However, the fact that various substances have been tried as substitutes for bismuth subnitrate for making radiographic examinations shows that this largely used preparation has not given entire satisfaction.

The use of bismuth subnitrate for radiographic examinations was advocated by H. Rieder in 1904, who stated that it displayed no injurious effect on the gastro-intestinal tract and was specially suitable for the examination of the digestive canal. For this purpose he recommends a bismuth meal of the following composition:

Two to three tablespoonfuls — about 30 grammes (1 oz) — of bismuth subnitrate are mixed with a little milk and this mixture is added to 300—400 grammes (10—14 oz) of flour paste; to avoid constipation it is advisable to add a little milk sugar to the mixture. This meal is readily taken, and according to the statements of patients has a somewhat chalky taste. Immediately after the administration of the meal the radiosopic or radiographic examination of the abdomen can be undertaken and repeated at fixed intervals, and the topographical and physiological conditions of the stomach and intestines studied. If the large intestine only is to be examined radiosopically it is not necessary to administer a meal containing bismuth; in this case the bowels are thoroughly emptied by an enema and a rectal injection of a mixture consisting of 1 litre (33 oz) of water, milk or oil and about 100 grammes ($3\frac{1}{3}$ oz) of bismuth subnitrate is given. According to Rieder, by means of a bismuth meal the size, form, position or displacement of the stomach can be exactly determined, as well as the motility of the stomach. Further, the various parts of the intestine can be reproduced more or less clearly on the photographic plate and from their position and shape important conclusions as to pathological changes may be drawn.

To diagnose the presence of cancer or stricture of the œsophagus Rieder employs a so-called “bismuth pill” which slowly descends the œsophagus and stops for some time on reaching a stricture, so that this spot can be localised on examination. The “bismuth pill” consists of about 2 grammes

Rieder, Münchener medizinische Wochenschrift 1904, No. 35, p. 1548. — Fortschritte auf dem Gebiete der Röntgenstrahlen Vol. 8, p. 133. — Münchener medizinische Wochenschrift 1906, No. 3, p. 111.

(30 grains) of bismuth subnitrate put in a wafer, or of a mixture of 10 to 15 grammes ($\frac{1}{3}$ — $\frac{1}{2}$ oz) of bismuth subnitrate and 50 grammes ($\frac{1}{2}$ oz) of water; this mixture slowly runs through the œsophagus towards the stomach and therefore its position can be seen on the photographic plate. If it passes too quickly through the stricture, A. Cahn recommends the use of a pill made of bismuth subnitrate and thick rice paste, which is held up in its progress in different positions of the œsophagus above the cardia and advances only after some time. For the diagnosis of œsophageal changes Jollasse also advocates the use of a thick paste in place of the pill, recommended by Holzknacht. A suitable paste is prepared by mixing 30 grammes (1 oz) of bismuth subnitrate and 15 grammes ($\frac{1}{2}$ oz) of milk sugar with a little water. According to the circumstances of the case or to suit the requirements of the radiographer the consistence of the paste may be varied at will. A different vehicle may be selected for the diagnosis of affections of the stomach and in studying the morphology and physiology of the stomach. According to F. M. Groedel a paste made of rice, flour, semolina or potatoes, spinach or minced meat may be used to suit the patient's taste. 40 to 50 grammes ($\frac{1}{3}$ — $\frac{1}{2}$ oz) of bismuth subnitrate are mixed with a little water or milk and sufficient paste is added to make 400 grammes (14 oz). For children correspondingly smaller amounts are employed, and raspberry syrup may be added to the meal; the bismuth subnitrate may be rubbed down with the syrup.

Groedel shares Rieder's view that bismuth subnitrate is a harmless substance, and only in the case of children demands caution as regards dosage. This is borne out by the fact that numerous examinations have been made with the aid of bismuth subnitrate and only rarely have slight secondary effects, such as vomiting, been observed. As already mentioned, these

Cahn, Münchener medizinische Wochenschrift 1906, No. 2, p. 73.
Jollasse, Münchener medizinische Wochenschrift 1907, No. 29, p. 1424.

Holzknacht, Wiener medizinische Wochenschrift 1906, No. 28, p. 1420. — Berliner klinische Wochenschrift 1906, No. 5, p. 127.

— Fortschritte auf dem Gebiete der Röntgenstrahlen Vol. 11, No. 1, p. 66.

Groedel, Münchener medizinische Wochenschrift 1907, No. 22, p. 1068.

toxic symptoms are most probably due to accessory circumstances, which cannot be foreseen or ascertained beforehand.

The harmlessness of bismuth subnitrate, however, was not accepted unchallenged, and later Groedel himself had to modify his original view. Already in 1906 Kaestle questioned whether the large doses recommended by Rieder might not cause unwelcome sequelæ, and for this reason he adopted the use of smaller doses. On internal administration he reduced the dose from 40—50 grammes ($1\frac{1}{3}$ — $1\frac{2}{3}$ oz) to 30 grammes (1 oz), and for rectal injection from 100 grammes ($3\frac{1}{3}$ oz) to 50—70 grammes ($1\frac{2}{3}$ — $2\frac{1}{3}$ oz) and added kaolin in order to keep the bismuth subnitrate better suspended. Later Kaestle, to avoid nitrite poisoning, made use of bismuth carbonate, and then abandoned the use of the latter in favour of thorium oxide. After the absolute harmlessness of bismuth subnitrate had been questioned by others and several cases of poisoning had been reported, inter alia by Barabasche, Eggenberger, Nowak and Gütig, Pape, Bensaude and Rivet, the use of bismuth subnitrate has been to some extent abandoned. However, it still numbers numerous adherents who use it on account of its power of casting dense shadows*.

Bismuth Sulphide.

Bismuth sulphide, Bi_2S_3 , is a brownish-black powder, insoluble in water and in dilute acids. Theoretically this substance answers the requirements to be made of a preparation for casting shadows, however, it has little prospect of being employed on a large scale. Its use was tried by C. Kaestle, who based his experiments upon the fact that bismuth compounds on internal administration are entirely or in great part

Kaestle, Münchener medizinische Wochenschrift 1908, No. 51, p. 2666.

Barabasche, Gazzetta degli ospedali e delle cliniche 1908, No. 110. Eggenberger, Zentralblatt für Chirurgie 1908, No. 44.

Nowak-Gütig, Berliner klinische Wochenschrift 1908, p. 1764.

Pape, Klinisch-therapeutische Wochenschrift 1913, p. 386.

Bensaude-Rivet, Münchener medizinische Wochenschrift 1909, p. 1053.

* Compare: M. Ehrenreich, Berliner klinische Wochenschrift 1913, No. 16, p. 734.

Kaestle, Münchener medizinische Wochenschrift 1909, No. 18, p. 919.

excreted in the faeces in the form of bismuth sulphide. It may be assumed that pure bismuth sulphide is not altered in the stomach and not absorbed in the intestine, provided that the substance used has been first carefully analysed. Apart from the purity of the preparation, care must be taken to establish the absence of any bismuth sulphate which may be formed during the storage of bismuth sulphide.

Kaestle did not observe any undesirable secondary effects after the administration of bismuth sulphide, although he frequently employed this substance. Owing to its brownish-black colour he abandoned its use, or used it only for rectal injections.

Cerium Oxide, Anhydrous

I have been unable to trace any mention of the use of cerium oxide in skiagraphy, but as I have received enquiries for information on this subject, a few remarks on this preparation may be opportune.

Pure cerium oxide, CeO_2 , is a heavy, faintly yellow powder, insoluble in water and in dilute acids; it is only dissolved by hot concentrated sulphuric acid. In my opinion it is too expensive for radiographic examinations, and therefore scarcely comes into consideration for this purpose.

The commercial product contains the oxides of lanthanum, neodymium and praseodymium as impurities and for this reason has a colour resembling that of rust. It is also practically insoluble in water and in dilute acids. It is considerably cheaper than pure cerium oxide, and the impurities mentioned above would not exclude its internal use in suitable doses. According to Kobert, the neodymium and praseodymium present as impurities are very slightly toxic, even if they were dissolved in the organism. Nothing definite can be stated regarding the behaviour of cerium should it be dissolved and absorbed in the organism, and in this connexion it may be mentioned that cerium oxalate is administered therapeutically in daily doses up to 1 gramme (15 grains). If, as has been stated, this preparation is insoluble in the organism and is not absorbed, how can the effects attributed to it in nervous affections and in cardialgia be explained? Baehr and Wessler have de-

Kobert, Intoxikationen 1906, II., p. 414.

Baehr-Wessler, Merck's Report 1909, p. 157.

monstrated that daily doses of 50 grammes of cerium oxalate given to dogs do not produce any injurious effects, and the oxalates of the impurities present in commercial cerium oxalate (Nd., Pr., La. and Th.) are also said to be non-toxic. On the other hand, Wassilieff, Löwenthal and Kobert state that soluble salts of cerium cause paralysis of the heart and nephritis, irritate the intestinal mucous membrane, and injure the red blood corpuscles, and therefore Kobert deprecates the use of these salts.

The possible use of cerium oxide would, therefore, depend upon the definite proof by pharmacological experiments of its innocuousness to the organism.

Iron Oxide.

According to K. Taege the now obsolete red iron oxide (Crocus martis adstringens) which was formerly used in medicine, may be used in place of magnetic iron ore. Calcined anhydrous iron oxide, Fe_2O_3 , is a reddish-brown powder, insoluble in water. It is very slowly and only in very small amounts soluble in very dilute hydrochloric acid; it is more soluble in concentrated hydrochloric acid. As it is a commercial preparation it is easily obtainable, and its purity can be established by analysis. Very small amounts only are dissolved in the gastric juice and the iron compound thus formed can scarcely prove injurious since larger doses of iron are usually administered for medicinal purposes. The experiments conducted by Taege with this substance showed that it possessed a satisfactory amount of shadow-casting power*.

The author directs that the dry iron oxide be mixed in a mortar with powdered tragacanth and the mixture transferred to a glass bottle with a wide mouth, in which it is well shaken with water. The quantity of tragacanth employed should amount to 1 p.c. of the total weight of the mixture. For rectal injection iron oxide may be used in an oily suspension.

Taege, Münchener medizinische Wochenschrift 1909, No. 15, p. 758 and No. 23, p. 1184.

* According to Kaestle (Münchener medizinische Wochenschrift 1909, No. 50, p. 2577) in order to obtain shadows of the same density as those cast by bismuth carbonate a larger quantity of iron oxide or ferroso-ferric oxide (magnetic iron ore) must be employed, viz., 3—4 times more.

C. Kaestle also made use of iron oxide, but he prefers anhydrous thorium oxide.

The above mentioned authors do not state the amount of iron oxide which should be used for examinations in man; Taege merely states that he has himself taken 50 grammes ($1\frac{2}{3}$ oz) of the substance in cachets without observing any effects.

Kaolin.

Kaolin, which is insoluble in water and in dilute acids, is known to be an innocuous substance which can be administered internally in any amounts, and has proved of great value in the treatment of enteritis, cholera, cholerae, etc.*. Kaolin should be an ideal substance for radiographic examinations of the stomach and intestine provided it were capable of casting a sufficiently dense shadow. Reliable data on this point are, however, not available in the literature at my disposal. Kaolin has sometimes been added to meals containing bismuth compounds, or barium sulphate, with the object of preventing the meal from settling too quickly, and the conclusion may be drawn that kaolin by itself does not possess shadow-forming power.

Magnetic Iron Ore.

Magnetic iron ore (Magnetite), a mineral principally occurring in Sweden, is chemically ferrous-ferric oxide, FeOFe_2O_3 . It is quite insoluble in water and in dilute mineral acids, and therefore may be administered internally in large doses, provided it is free from other soluble or poisonous compounds. In addition to iron, commercial magnetite contains magnesium, manganese, chromium, aluminium, nickel and titanium. Arsenic would only be present by chance or owing to a mistake. Under no circumstances, however, should commercial magnetic iron ore be used for radiographic examinations without being first carefully analysed. In purchasing powdered magnetite the identity of the preparation should first be chemically established; further, whether on boiling with dilute hydrochloric acid any soluble compounds are formed, and if so, whether these soluble compounds

Kaestle, Münchener medizinische Wochenschrift 1909, No. 18, p. 919.

* Compare Merck's Reports 1905—1912.

are poisonous. Experience has shown that it is impossible to be too careful in using substances for radiographic examinations*.

The use of magnetic iron ore as a substitute for bismuth salts was suggested by L. Lewin. He states that this mineral is almost insoluble in the gastro-intestinal tract, and can be added to pasty meals in the form of a fine powder. Large amounts of it can be employed and the colour of the mixture serves as an indication of the quantity added. According to the amount added, potato meal assumes a greyish to black colour. As some patients object to take a black mixture with a somewhat unappetising appearance, the use of chocolate as a vehicle, suggested by the author, presents the best means of avoiding this objection.

The animal experiments conducted by Lewin showed that feeding with magnetic iron ore caused no alteration in the condition of the animals, and the appetite remained unaffected. Magnetic iron ore is said to possess a considerable shadow-casting power; at least trials in man have yielded very clear pictures.

As regards the fineness of the powder employed, it should be sifted through a sieve containing 5000 meshes to each square centimetre.

W. Alexander elaborated the clinical use of this method. He states that powdered magnetic iron ore (a black powder resembling charcoal) is odourless and tasteless, but, given in suspension in water, leaves in the mouth a sandy sensation. As it cannot be given in water owing to the fact that it quickly settles, and presents an unappetising appearance when mixed with potato meal, while in the form of a chocolate pudding the patients are unable to take it in sufficient amount, the author makes use of a mixture of magnetic iron ore, powdered salep, milk sugar and cocoa**, which is placed on the market

* Compare the discussion on the paper read by Alexander in the *Deutsche medizinische Wochenschrift* 1909, No. 19, p. 870. Lewin, *Münchener medizinische Wochenschrift* 1909, No. 13, p. 644. Alexander, *Deutsche medizinische Wochenschrift* 1909, No. 20, p. 877.

** These mixtures have the drawback that they cannot be tested with the same facility as magnetic iron ore per se. For this reason substances used for radiographic examinations should be purchased unmixed, and after determining their purity, they are mixed as required.

under the name of "diaphanit". On mixing this with hot water the powdered salep yields a mucilaginous vehicle which prevents the magnetic iron ore from settling too quickly, the addition of milk sugar is intended to counteract the possible constipating action of magnetic iron ore while the cocoa imparts a palatable taste to the mixture. The author states that on mixing his preparation with hot water a beverage is produced which does not differ in taste from ordinary cocoa, but in appearance is somewhat darker. The sandy taste can be effectively masked by eating biscuits. The ingestion of this meal is not followed by any symptoms whatever; only patients suffering from diseases of the stomach who have for some time been accustomed to take only a small amount of food experience a feeling of fulness. In no case was the patient's condition adversely affected by taking this meal, and the urine remained free from pathological products; only the stools were black and dry for two or three days. However, the author did not observe a definite constipating effect.

The shadow-casting power of magnetite is inferior to that of bismuth salts, and in order to obtain the same effects it is necessary to employ larger quantities of the former. The author employed for an examination of the stomach 150 to 200 grammes ($5-6\frac{2}{3}$ grains) of diaphanit and 300 grammes (10 oz) of water; this amount corresponds to 100 to 140 grammes ($3\frac{1}{3}-4\frac{2}{3}$ oz) of magnetic iron ore. For rectal injection be made use of 300—350 grammes (10 to $11\frac{2}{3}$ oz) of diaphanit without the addition of cocoa and milk sugar, i. e., a mixture of magnetic iron ore and powdered salep only. Before giving the injection the bowel should be emptied.

Manganese Oxide.

Several years ago Günther referred to manganese oxide as being a preparation which might be used for radiographic examinations. The composition of manganese oxide, Mn_2O_3 , is analogous to that of iron oxide. It occurs as a black powder, almost insoluble in water and very dilute acids; it

Günther, Paper read at the meeting of the niederrheinische Gesellschaft für Natur- und Heilkunde in Bonn, December 12, 1910. Compare Deutsche medizinische Wochenschrift 1911, No. 15, p. 177.

dissolves in concentrated hydrochloric acid. In this respect it resembles manganese dioxide, MnO_2 . I have been unable to trace any mention in the literature regarding the use and suitability of these two substances. The black colour of both substances is a drawback, even should they be found on investigation to prove suitable for radiographic examinations.

Red Mercuric Sulphide (Cinnabar).

Among the substances which have been utilised for radiographic examination of the gastro-intestinal tract, cinnabar occupies a very secondary position. The fact that it is almost completely insoluble in acids and alkalies and also in the juices normally present in the stomach and intestine, coupled with its behaviour towards X-rays, would make this preparation highly suitable for this purpose, provided it is first carefully tested to establish its purity. However, there will always be a certain amount of objection to the use of a preparation of mercury. With the use of cinnabar the possibility of toxic symptoms supervening would be primarily due to the products produced by its possible oxidation, and not to the partial solubility or absorption of the unaltered substance itself. C. Kaestle tested the suitability of cinnabar for radiographic examinations and states that it has drawbacks, without going into details. In his opinion anhydrous thorium oxide is in every respect superior to cinnabar.

Thorium Oxide, Anhydrous

Thorium oxide, ThO_2 , is a heavy white powder, insoluble in water, acids and alkalies. Only on heating with fuming sulphuric acid can it be converted into soluble thorium sulphate. As thorium oxide is very opaque to X-rays it is an extremely suitable substance for skiagraphic work, provided a pure preparation be employed. According to C. Kaestle, the possibility of toxic symptoms occurring after the internal use of this substance* is quite excluded. Further, relatively small amounts cast a dense shadow, which shows greater contrasts than obtainable with the same amount of bismuth subnitrate or

Kaestle, Münchener medizinische Wochenschrift 1908, No. 51, p. 2667.

Kaestle, Münchener medizinische Wochenschrift 1908, No. 51, p. 2666 and 1909, No. 18, p. 919.

* The author employed Merck's anhydrous thorium oxide.

bismuth carbonate. Experiments on dogs and cats showed that thorium oxide passes unchanged through the gastrointestinal tract and does not display any effect on the organism; in fact the amount of thorium oxide administered can be recovered in toto from the fæces. The author gave intra-gluteal injections of several grammes of the substance to animals which were kept under observation for periods varying from several weeks to two months and was unable to observe the occurrence of any toxic symptoms whatever. Small animals, e. g., a dog weighing 5 kilogrammes, were given repeatedly as much as 80 grammes of thorium oxide per os with no untoward effects, even defæcation was not influenced in any way. Kaestle was also able to confirm the usefulness of anhydrous thorium oxide in man, and he recommends its use per os, or for rectal injection, in the form of an aqueous suspension with kaolin. According to the total amount of the mixture required, the ratio of thorium oxide to kaolin is as 1:3, or 1:4. For adults 20 to 30 grammes ($\frac{2}{3}$ —1 oz) are required for internal administration. For rectal injection in children of twelve years of age 10 to 15 grammes ($\frac{1}{3}$ — $\frac{1}{2}$ oz) of thorium oxide are sufficient. Thorium oxide itself is tasteless, but if an aqueous suspension of thorium oxide and kaolin is not readily taken, the thorium oxide may be given in a meal, stewed fruit, or in kephir.

Although it is theoretically quite impossible that even traces of thorium oxide might be dissolved in the body, yet this possibility deserves consideration in the event of traces being dissolved under unforeseen circumstances. Thorium salts have so far not been investigated pharmacologically to any great extent, but they can scarcely be regarded as dangerous. Kobert states that the experiments made in his institute with thorium showed that it possesses only a slight toxic action. The experiences of S. Tracy are in agreement with this result; he prescribed a 25 p.c. thorium nitrate* ointment in the treat-

Kobert, Intoxikationen 1906, II, p. 414.

Tracy, Medical Record 1904, January 23. — Merck's Reports 1904, p. 189.

* The use of thorium nitrate for inhalation in the treatment of pulmonary tuberculosis, suggested by E. Rutherford (Klinisch-therapeutische Wochenschrift, 1904, No. 9), S. Tracy (l. c.) and Gordon Sharp (British Medical Journal, 1904, I, p. 654), cannot be regarded as a proof of the non-toxic nature of thorium ni-

ment of cutaneous diseases. Therefore it is apparent that thorium oxide may be included among the safest substances for use in radiographic examinations.

Tungsten, Colloidal

R. Krüger recommends the use of colloidal tungsten in the place of bismuth salts for the radiographic examination of the gastro-intestinal tract. This substance occurs as a black, odourless and tasteless powder. Von Hayek's investigations showed that it is entirely non-toxic, and this was confirmed by Krüger by experiments in rabbits. He administered to rabbits by means of an oesophageal tube 5 to 25 grammes of the preparation. The animals did not show any symptoms of illness, they ate well and showed no difference in their behaviour. The author thereupon tried the preparation in man, in doses of 25 to 80 grammes, and in no case did he observe the occurrence of toxic symptoms; none of his patients showed signs of gastric or intestinal disturbances, stomatitis or nephritis. A comparison of the radiographs taken of the same person with bismuth and with tungsten exhibited no difference, in both cases the outlines of the stomach were equally clear. (From Merck's Annual Report, 1912.)

Zirconium Oxide, Anhydrous

Zirconium dioxide, ZrO_2 , is a heavy white powder, practically insoluble in all acids*. Only hot sulphuric acid and hydrofluoric acid gradually act upon it. According to C. Kaestle bismuth salts, magnetic iron ore and iron oxide cannot compare with calcined zirconium oxide as regards insolubility. Zirconium oxide undergoes no alteration whatever

trate, since it is not the salt itself but its emanation which is used for inhalation; the organism, therefore, is not required to absorb this soluble salt of thorium.

Krüger-Hayek, *Münchener medizinische Wochenschrift* 1912, No. 35, p. 1910.

* A cheap zirconium oxide, which is certainly a mineral zirconia, is issued under the name of "Kontrastin". As is the case with all preparations used for radiographic examinations, the determination of its purity by chemical means prior to use is a *sine qua non*.

Kaestle, *Münchener medizinische Wochenschrift* 1909, No. 50, p. 2576.

in the animal and human organism; it passes through the gastro-intestinal tract unchanged and is excreted in the ordinary way, without any subjective or objective deviation from the normal condition. Kaestle was able to confirm this by numerous trials in animals and in man.

As the zirconium compounds have as yet not been subjected to exhaustive pharmacological tests, the author investigated the action of zirconium oxide on animals. He injected into rabbits (into the glutei) several grammes of zirconium oxide, and found that after eight months the preparation was present at the site of injection, which healed without any reaction. The experimental animals remained perfectly normal, they gained regularly in weight and the urine did not contain any casts or albumin. He also gave to animals subcutaneous injections of solutions of zirconium salts in amounts corresponding to 0.4 gramme of zirconium per kilogramme body-weight. He was unable to observe any action whatever, and the post-mortem examination of the animals showed that the glandular organs and the intestines were normal. He repeatedly administered internally to animals 1 gramme of zirconium solution per kilogramme body-weight, even as much as 2 grammes of readily soluble zirconium oxychloride per kilogramme body-weight to a dog, without ever observing the slightest effects from this treatment. From these observations it may be concluded that the soluble salts of zirconium, even if absorbed in large doses, are non-toxic and free from any action. The result of Kaestle's investigations is all the more striking in view of the fact that in rabbits the absorption of 0.03 gramme of bismuth is sufficient to cause death.

These results show that insoluble zirconium dioxide is an ideal substance for skiagraphic work. Its value for this purpose is further enhanced by the fact that it is considerably superior to iron oxide in shadow-casting power, and almost equal to bismuth carbonate in this respect. While compared with magnetic iron ore it not only has the advantage of greater opacity but also that of not imparting a colour to the mixture employed.

For examination of the stomach a mixture of 1 part of zirconium dioxide and 0.5 or 1 part of kaolin is employed, suspended in the requisite amount of water. For rectal injection a mixture of 150 to 200 grammes (5—7 oz) of zirconium

dioxide and 200 grammes (7 oz) of kaolin suspended in 1 litre (33 oz) of lukewarm water is used. For internal administration doses of 75 grammes ($3\frac{1}{2}$ oz), and for rectal injection 200 grammes (7 oz) may be exceeded without apprehension. However, it is imperative to employ pure zirconium dioxide, or a preparation which is free from toxic substances. If, for reasons of economy, the cheaper technical products are used, care must be taken to establish the absence of arsenic in the zirconium oxide supplied for this purpose. A case has come to my knowledge in which the use of a commercial product containing arsenic almost cost the patient his life. In this case, as well as with all substances used for radiographic examinations, the preparation should first be submitted to careful analysis, and by observing this very necessary precaution unpleasant surprises may be avoided. By the use of a substance containing poisonous impurities an otherwise innocuous and useful preparation for radiographic examinations may easily be discredited.

Preparations and Drugs.

Abrus Precatorius.

In my last year's Report brief mention was made of the treatment of carcinomatous affections by jequirity, first proposed by Rampoldi. C. Chiri deals exhaustively with the value of this method, and reports a case of a woman, aged 67, who had a sluggish, suppurating ulcer of the nose (and an ulcer on the cheek) which on histological examination proved to be an epithelioma. Jequirity ointment and gelatin discs containing jequirity were applied alternately to the ulcers, removing the crusts before each application; during the first few days the serous discharge and the formation of crusts increased, but the repeated application of the remedy led to necrosis, and finally to a cure. The cosmetic effect was also highly satisfactory, since both ulcers healed without leaving scars. Chiri insists on the importance of this method in the treatment of ulcerating epitheliomata. Should the application of the gelatin discs containing jequirity cause too violent a reaction, the latter may be substituted for a time by the use of jequirity ointment.

C. Clerici also used jequirity with good results in three cases of epithelioma of the skin. Healing took place in the course of two months, leaving a smooth scar. The author considers the method too dangerous for cancroids situated in the mouth, or entrance to the uterus. On the other hand, it is apparently useful also in tuberculous wounds which refuse to heal.

Acitrin.

Acitrin, as already stated in last year's Report, is the ethyl ester of phenylcinchonic acid (of atophan). The preparation was tested by G. Pietrulla with a view to establish whether it displayed the same action on the excretion of uric acid and the same clinical effects as the free

Rampoldi, Merck's Report 1912, p. 72.

Chiri, *Gazzetta degli ospedali e delle cliniche* 1913, No. 106, p. 1103.

Clerici, *Rivista Medica (Milano)* 1913, p. 79.

Pietrulla, *Deutsche medizinische Wochenschrift* 1913, No. 8, p. 359.

acid*. For this purpose he administered acitrin to healthy persons and to individuals affected with rheumatism and gout, and found that a daily dose of 3 grammes (45 grains) of the drug immediately produced a considerable increase in the excretion of uric acid in healthy as well as sick persons, such as is also the case with atophan. However, the observation was made that while the continued administration of acitrin to a healthy person caused great variations in the excretion of uric acid, the amount excreted by a gouty subject remained high and only varied between 0.7 and 1.0. A sick person who had been unsuccessfully treated for several weeks by other remedies showed an improvement when placed on a diet poor in purins, the pains diminished, the joints became less sensitive to pressure, the swellings decreased and the tophi became smaller. The patient, who had formerly been confined to his bed, was now able to resume his occupation and enjoyed good health.

The use of acitrin proved equally successful in other cases, in which an estimation of the amount of uric acid excreted was not practicable. These results show that acitrin displays the same action as atophan. No injurious effect on the general health was observed, and the gastric function was never disturbed.

Impens states that the action of acitrin is somewhat more prolonged than that of atophan, and the greatest excretion of uric acid takes place between three to six hours after its ingestion, whereas with atophan this takes place already within the first three hours following its administration. In order to obtain the greatest possible therapeutic effect it is advisable to give acitrin in repeated doses, and to administer at least a total amount of 2 grammes (30 grains) daily.

According to M. Dohrn the pharmacological action of acitrin differs from that of atophan inasmuch as it does not possess any antiphlogistic effect. The author attributes this to the esterification of the carboxyl** group present in atophan.

* Compare Atophan, Merck's Reports 1911 and 1912.

Impens, Archives internationales de pharmacodynamie et de thérapie 1912, Vol. 22, p. 379.

Dohrn, Therapie der Gegenwart 1913, No. 5, p. 196.

** Compare Merck's Report 1911, p. 162.

Adalin.

The sedative and hypnotic action of adalin* was thoroughly investigated by Uhlmann in mental diseases, such as dementia præcox, manic-depressive insanity, paralytic dementia, dementia senilis, melancholy, hysteria and epilepsy. His experience, which extended to a large number of cases, showed that the doses hitherto employed to obtain a sedative effect are too small, and in several instances he administered as much as four doses of 0.5 to 0.75 gramme ($7\frac{1}{2}$ —12 grains) of adalin in order to obtain a satisfactory action. In some cases he was obliged to combine the administration of four doses of 1 gramme (15 grains) of adalin with the same number of doses of 0.3 to 0.5 gramme (5 — $7\frac{1}{2}$ grains) of luminal, or with large doses of veronal, trional, paraldehyde, etc. In about 70 p. c. of his cases four daily doses of 0.5 gramme ($7\frac{1}{2}$ grains) of adalin and one dose at night of 1 gramme (15 grains) proved sufficient; 13 p. c. required doses of 0.75 gramme (12 grains); 7 p. c. reacted only after 1 gramme (15 grains); 9 p. c. required a combination of adalin and other hypnotics; and 1 p. c. showed no reaction whatever.

In about 90 p. c. of the cases the effect set in only from the second or third day. The action was generally good in dementia præcox, whereas in manic-depressive insanity a prompt effect was displayed only in a few cases. As regards the ratio of the action to the severity of the disease, of 129 slight and moderate cases 128 reacted well or fairly well to doses of 0.5—0.75 gramme ($7\frac{1}{2}$ —12 grains); of the 17 severe cases only 6 reacted well. Therefore, the latter do not respond well to this treatment.

To obtain a hypnotic action larger doses (1—2 grammes) (15—30 grains) were required; these, however, yielded satisfactory results in almost every case. The observation made by the author that habituation does not occur speaks in favour of adalin, as well as its freedom from unwelcome secondary effects.

Löbinger prescribed adalin to combat sleeplessness due to chronic bronchitis and emphysema associated with severe

* Compare Merck's Reports 1910—1912.

Uhlmann, Psychiatrisch-neurologische Wochenschrift 1912, No. 35.

Löbinger, Allgemeine medizinische Zentralzeitung 1913, No. 4, p. 40.

nightly asthmatic attacks, and also in sleeplessness due to pains in the region of the heart. In the former he gave in the morning and afternoon 0.5 gramme ($7\frac{1}{2}$ grains), and at 8 p.m. 1 gramme (15 grains) of adalin, whereupon at 10 p.m. sleep lasting five to six hours was induced; in the latter cases he administered 1 gramme (15 grains) at night. In both cases the effect was highly satisfactory. In the author's experience adalin displays the best action if it is given exactly two hours before going to bed. This observation is probably due to the fact that owing to the slowness with which it dissolves adalin displays its effect some time after its ingestion.

Induced by a statement made by Philippssohn, R. Blumm tried adalin in a patient who immediately passed watery stools on partaking of hot or cold foods and beverages. Other remedies had proved unsuccessful, but a daily dose of 0.5 gramme ($7\frac{1}{2}$ grains) of adalin effected a cure. However, after an interval of several weeks this treatment had to be resumed for three or four days as soon as the stools commenced to become thinner, which was especially the case before the onset of menstruation. On the basis of the foregoing observation, adalin may prove useful in the treatment of nervous diarrhoea.

Adalin cannot be said to be absolutely harmless, as is apparent from a statement by Siebelt. He states that a healthy man, aged 37, took 2 grammes (30 grains) of adalin at one dose; this was followed by delirium, loss of consciousness, accelerated respiration, and small, quick pulse. The patient recovered after an injection of 0.2 gramme (3 grains) of camphor. This case urges caution in the dosage of adalin, as, according to the author, the possibility of an idiosyncrasy to the drug was excluded in this instance.

Adamon.

During the past year reports on the therapeutic use of adamon (dibromo-dihydro-cinnamic acid borneol ester)*

Philippssohn, Medizinische Klinik 1911, No. 53, p. 2052.

Blumm, Münchener medizinische Wochenschrift 1913, No. 18, p. 1014.

Siebelt, Deutsche Ärzte-Zeitung 1913, No. 19, p. 289.

* Compare Merck's Report 1911 and 1912.

were published by H. Gudden, H. Oppenheim and Treitel.

Gudden regards adamon as a substitute for preparations of valerian, over which it has the advantage of being a solid compound and is free from any unpleasant taste, therefore it does not cause the disagreeable eructations produced by valerianic acid and its esters. He used adamon in the usual indications for preparations of valerian, i. e., in general nervous troubles, neurasthenia and hysteria, and also in nervous affections of the heart, such as nervous tachycardia, dyspnoea, and in nervous disorders of the female sexual functions. It proved particularly useful in delusions, but it failed in epilepsy.

Gudden reports that adamon displayed a prompt sedative action in most of his patients, leading to an abatement of the intense excitement and restlessness. The fear and vertigo diminished, and the prolonged use of this remedy led to such an improvement that the patients were again able to sleep and resume their occupations. The author found that repeated small doses of 0.5 gramme ($7\frac{1}{2}$ grains) displayed a more favourable effect than the administration of a single large dose. For this reason he prescribed, as a rule, one adamon tablet three to four times a day, to be taken after meals, in weak tea or hot lemonade, as well as three tablets to be taken before going to bed. Adamon does not possess a pronounced hypnotic action like veronal, and cannot compete with the latter in this respect; on the other hand its use may prove valuable in preventing a possible misuse of hypnotic drugs.

Oppenheim arrived at similar conclusions. He also found that the administration of small doses is, as a rule, to be preferred to the use of large single doses. He obtained the best effect by giving single doses of 0.5 to 1 gramme ($7\frac{1}{2}$ to 15 grains) at intervals of one to two hours. He regards it as advisable to gradually increase and decrease the amount administered until the active total daily dose is reached, which is then maintained for a longer or shorter period, as required. This method is particularly suited for prolonged

Gudden, Medizinische Klinik 1913, No. 4, p. 137.

Oppenheim, Deutsche medizinische Wochenschrift 1913, No. 23, p. 1103.

Treitel, Berliner klinische Wochenschrift 1913, No. 4, p. 168.

treatment. In numerous cases of disturbances at the menopause Oppenheim obtained very satisfactory results, and adamon proved particularly useful in general nervous excitement associated with restlessness during the night, terrifying nervous dreams and nightmare, and also in flushings of heat, in itching and burning at the genitals, feeling of oppression in the chest, pressure on the head and vertigo. With increasing improvement in the general condition the symptoms accompanying these disturbances also disappeared, such as nausea, loss of appetite, feeling of fulness in the stomach, weight in the legs, etc.

Like Frank, Oppenheim also tried the action of adamon as an anaphrodisiac, and in 80 per cent. of the cases, particularly in sexual irritability in the years preceding the menopause and in nymphomania, further in artificially induced menopause (by double oöphorectomy) and to combat excitement before and after operative procedures, he obtained good results.

E. Junger reports good results with adamon as a hypnotic and sedative in some functional disturbances, such as neuroses, neurasthenia, and in alcoholism. However, he does not consider it to be superior to the older remedies.

The use of adamon deserves consideration in the treatment of conditions of irritability in acute gonorrhœa. Treitel employed it in 40 cases in which nightly erections and pollutions were present, and usually obtained an appreciable alleviation of the troubles already after the first dose. He administered adamon in tablets, to be taken in water, and made his patients take two tablets of 0.5 gramme ($7\frac{1}{2}$ grains) between 5 and 6 p. m., and two tablets about half an hour before going to bed.

Adonidin and Adonis Vernalis.

Opinion regarding the therapeutic value of Adonis vernalis* as a cardiac tonic is at present divided as a result of the investigations carried out during recent years by different observers. Thus, while Henrijean and Honoré maintain that the drug is a useful cardiac tonic which increases

Frank, Merck's Report 1912, p. 79.

Junger, Prager medizinische Wochenschrift 1913, No. 36.

* Compare Merck's Report 1911, p. 75.

the blood pressure and regulates the action of the heart, Lemoine and Henneton concede that it acts as a cardiac tonic and diuretic, but state that it has no action on the blood pressure. Roch even believes that adonis acts merely as an emetocathartic with a slight action on the heart. A work by J. Chevalier on this point is therefore of interest.

Chevalier believes that the varying results observed by the authors mentioned above are due to differences in the content of active principles in the preparations employed, and therefore again undertook a study of the drug. He was able to confirm the findings of Fückelmann, viz., that the glucoside placed on the market under the name of adonidin is a mixture of adonidinic acid and neutral adonidin. According to Chevalier both substances possess properties similar to those displayed by saponins*. They display a local irritant action, especially in the intestine, produce hæmolysis, this is particularly the case with adonidinic acid, exert an action on the heart and exhibit a diuretic effect. They are readily decomposed, especially by acids, and lose a part of their activity in the course of preparation. Chevalier attributes the differences in action which have been observed to this ready decomposition of the drug, and for this reason he is of opinion that the fresh plant and the preparations made from it (tinctures and extracts) display the greatest activity.

His trials with adonidinic acid and neutral adonidin show that both preparations act as cardiac tonics; however, adonidinic acid is more toxic and 1.3 times more active than neutral adonidin. The author is of opinion that the action of adonis resembles more closely that of squill than that of digitalis. At least his results show that the diuretic effect of adonis is similar to that of squill and is due to irritation or stimulation of the kidneys. The selective action of adonis

Roch, *Semaine médicale* 1911, No. 46, p. 541; 1913, No. 39, p. 460.

Chevalier, *Nouveaux remèdes* 1913, No. 3, p. 49.

Fückelmann, *Merck's Report* 1911, p. 79.

* Professor Kobert in a communication to me states: In my saponin table (*Beiträge zur Kenntnis der Saponinsubstanzen*, 1904) in the members of the series $C_n H_{2n-8} O_{10}$, between C_{15} and C_{26} , a single member is missing, i. e., $C_{25} H_{42} O_{10}$; this missing member appears to be adonidin. Therefore, of the substances of the digitalin group three are already characterised by their formulas as saponins, viz., gitalin, adonidin and helleborein (compare Sieburg, *Archiv der Pharmazie*, 1913, p. 154).

on the latter makes its use appear indicated in cases where digitalis has failed.

When prescribing the galenical preparations of adonis, a fact established by B. Slowzow must be taken into consideration. This author found that the toxicity of alcoholic extract of adonis is 1.5 times greater than that of the aqueous extract.

According to Schtschukin and Breitmann adonis is useful in the treatment of gastro-intestinal arterio-sclerosis. Schtschukin states that its diuretic effect is even superior to that of theobromine sodium salicylate. The author prescribed the following mixture with very satisfactory results:

Infus. Adonis vern.	8—10: 180 grammes (120—150 grains to 6 oz)
Codein. phosph.	0.02—0.25 gramme ($\frac{1}{3}$ —4 grains)
Tinct. Valerian. æther.	8 grammes (170 min.)

M. Sig.: 1 tablespoonful to be taken three times a day (in milk).

Breitmann confirms the value of adonis treatment. He reports cases of "abdominal angina" in which adonis was the only remedy which was well tolerated even when administered for several years, and it did not give rise to secondary effects (of course, the drug was not given continuously). Disturbances of digestion are comparatively rare, and may be easily avoided by adding 8 grammes (160 min.) of tincture of condurango to the above mixture. The good results reported by Breitmann may be due to the fact that he prescribed the liquid extract in daily doses of 1 to 2 grammes (17—34 min.), in the place of the infusion employed by Schtschukin.

Aesculin.

An article by L. Freund has awakened general interest in aesculin so that a brief description of this preparation, which has hitherto been used in therapeutics only in exceptional cases, may prove opportune.

Slowzow, Russkij Wratsch 1912, p. 1.

Schtschukin, Semaine médicale 1913, No. 6, p. 67.

Breitmann, ibid. 1913, No. 25, p. 295.

Freund, Wiener klinische Wochenschrift 1911, No. 19, p. 670.

Aesculin, which has been described in detail by Rochleder, Schiff, Minor and Trommsdorff, is obtained from the bark of *Aesculus Hippocastanum*. It occurs in small white crystals, which are sparingly soluble in cold water; the resulting solution has an acid reaction. It has the composition $C_{15}H_{16}O_9 + 1\frac{1}{2}H_2O$. It is more readily soluble in alkalies, boiling water and in hot alcohol. Its aqueous solutions, even very dilute solutions, have an intense blue fluorescence, which disappears on the addition of acids and reappears when the solution is made alkaline. On the whole, aesculin is a very stable glucoside and is not altered on boiling with weak bases. For instance, it can be boiled with a suspension of magnesia in water, with which it forms an additive compound. The latter, which has the composition $C_{15}H_{16}O_9 \cdot Mg(OH)_2$, is readily soluble in water and may be obtained in a dry state by evaporating the solution. It possibly deserves special interest as an adjuvant in the treatment of affections demanding protection from light, owing to the fact that it is readily soluble in water and exhibits a strong fluorescence. On boiling with strong alkalies, e. g., solution of barium hydroxide, or with mineral acids, aesculin is split up into aesculetin and glucose.

To my knowledge the first use of aesculin was based upon its property, in common with all fluorescent substances, of absorbing ultra-violet rays, which are then gradually given off. G. H. Graham made use of subcutaneous injections of aesculin as adjuvants to the Finsen light treatment of lupus vulgaris. For this purpose he injected 0.3 c. c. of an aqueous solution of aesculin containing 2 to 3 per cent. of sodium carbonate immediately beneath the skin to be treated by the Finsen light. The author states that the action produced by irradiation was more protracted than was the case without the use of aesculin. Graham was unable to observe any harmful secondary effects due to the injections of aesculin.

Rochleder, Liebigs Annalen der Pharmazie 1853, Vol. 87, p. 186 and Vol. 88, p. 356.

Schiff, *ibid.* 1872, Vol. 161, p. 71.

Minor, Archiv der Pharmazie 1900, Vol. 38, p. 130.

Trommsdorff, Liebigs Annalen der Pharmazie 1835, Vol. 14, p. 189 and 205.

Graham, Lancet 1905, II., p. 1769.

The use of aesculin in sunburn and as a prophylactic in blinding snow light, introduced by Freund, is also based upon the property of this substance of absorbing ultra-violet rays.

As a protection against the damage done to the skin by rays which have a short wave-length a number of remedies, generally dyes or highly coloured substances, had been used or tried with more or less success. Freund reports that an Indian officer made use of orange coloured material to avoid the painful effects of the light upon the skin. Unna prescribed the use of glycerin or casein ointments coloured with turmeric, ichthyol or Armenian bole, as these can easily be removed by washing with water. Veiel recommended the use of coloured gelatin, rouges and skin varnishes. According to Freund yellow vaseline also absorbs a small amount of ultra-violet rays, but is not suited for practical purposes as it would have to be applied in a very thick layer, and the addition of zinc oxide or white lead does not assist its action. The use of caramel, even in a thick layer, does not afford much protection from light.

A greater protection against light is afforded by quinine sulphate, the use of which was suggested by Hammer. As is well-known, aqueous solutions of this salt, to which a little sulphuric acid has been added, show an intensely blue fluorescence. The use of a solution of this kind is open to objection due to the action on the skin of the free sulphuric acid, especially on drying. Aesculin, according to Freund, is an extremely useful remedy for this purpose since it is free from any injurious action, as is apparent from Graham's observations, mentioned above. It is a powerful absorbent of ultra-violet rays, which are converted by it into a variety of light possessing another form of energy, the activity of which cannot be demonstrated by physiological means.

The investigations of Freund have shown that a 1—2 p. c. solution of aesculin in water or glycerin in a layer only 0.2

Freund, Zeitschrift für neuere physikalische Medizin 1908, Vol. 2, No. 2.

Unna and Veiel, communicated by Freund, comp. Blochs Praxis der Hautkrankheiten.

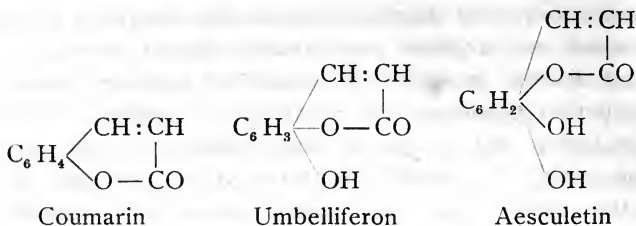
Hammer, Verhandlungen der deutschen dermatologischen Gesellschaften 1908.

millimetre thick still displays a powerful absorbent action and is therefore an excellent prophylactic against sunburn. As it does not dissolve in sufficient quantity at ordinary temperature, the author recommends the addition of colloidal substances, such as starch and gelatin, to the solution, so that when the solution cools the aesculin is retained in colloidal division with the result that the cooled mass still exhibits the powerful absorbent action on ultra-violet rays which is characteristic of aesculin. For instance, a preparation may be made up on the same lines as glycerin of starch, by mixing in a mortar 10 grammes ($\frac{1}{3}$ oz) of starch, 10 grammes ($\frac{1}{3}$ oz) of water, 2 to 4 grammes (30—60 grains) of aesculin and, if necessary, 8 drops of a 10 per cent. solution of sodium carbonate, and adding this mixture, with constant stirring, to 100 grammes ($2\frac{2}{3}$ oz) of glycerin heated to 110° C. until the mass becomes transparent and has the consistence of an ointment. The small addition of sodium carbonate increases the absorptive power of the mixture, and its protective effect is said by Freund to be even greater than that of ultrazeezon (see below). For practical use a 4 per cent. aesculin-glycerin ointment is to be preferred; it is best applied with a finger to the parts of the skin to be protected, and the use of a brush or pad is to be avoided for applying the ointment. The ointment adheres to the skin for several hours even on exposure to the wind, as on tours, and as it is colourless its presence is not noticeable; it is easily removed by washing with water and does not injure the skin.

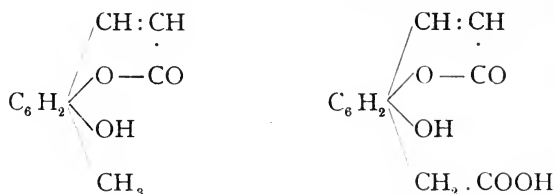
The cleavage product of aesculin, aesculetin, also possesses a powerful absorbent action on ultra-violet rays, and according to C. Mannich it is even superior in this respect to aesculin. From this fact the author concludes that the absorbent property of aesculin is not due to its sugar constituent but to the aromatic residue. Aesculetin, however, is chemically nearly related to coumarin and umbelliferon, as was demonstrated by Hlasiwetz.

Mannich, *Therapeutische Monatshefte* 1913, No. 2, p. 124. — *Berichte der deutschen chemischen Gesellschaft Berlin* 1909, Vol. 19, p. 388.

Hlasiwetz, *Berichte der deutschen chemischen Gesellschaft Berlin* 1871, Vol. 4, p. 550.



These substances and several of their derivatives also possess the property of absorbing ultra-violet rays, as is apparent from the results of investigations carried out by Mannich. Coumarin itself possesses this property only in a slight degree, but this property is displayed to a much greater extent by its hydroxyl, amido, phenyl and carboxyl substitution products; indeed, aesculetin, which has a very powerful absorbent action, is coumarin with two hydroxyl groups attached to its nucleus, as is apparent from the formulas given above. As a prophylactic against the effects of light, Mannich selected from among the above mentioned derivatives of coumarin β -methyl-umbelliferon and β -umbelliferon acetic acid,



both of which are colourless substances, soluble in water in the presence of alkalies, and which possess powerful absorbent properties. P. G. Unna undertook practical experiments with some of the substances named. He obtained highly satisfactory results from the use of a 10 per cent. dimethyl-amidocoumarin varnish in a case of intractable eczema of the face, with a 10 per cent. mono-oxycoumarin-eucerin ointment in a case of psoriasis with seborrhœic eczema, and in sunburn, etc., with a glycerin ointment containing a di-oxy derivative.

Under the designations zeozon and ultrazeozon pastes and ointments are issued, the exact composition of which is not given in the literature; zeozon is stated to contain 3 per cent.,

and ultrazeozon 7 per cent., of active substance, i. e., methylumbelliferon and umbelliferon acetic acid*.

M. Klotz employed the zeozon preparations in children to prevent erythema from sunlight in the insolation treatment of tuberculous children. His results show that the 3 per cent. zeozon paste is not capable of affording an absolute protection against the action of the midsummer sun, especially in delicate children and infants. On the other hand, after applying a thick layer of 7 per cent. ultrazeozon all the children may be exposed to the summer sun, without having to fear the occurrence of any forms of dermatitis from the action of the sunlight.

Afridol.**

Peters recommends afridol soap as a good antiseptic for the hands of surgeons and midwives. The author has used it in a large number of gynaecological and obstetrical operations. The hands are first washed with the soap, which is then removed by washing with water. Thereupon the hands and forearms are rubbed with the soap until a thick lather is produced, which is well rubbed into the skin. After this treatment of the hands curettage can be undertaken without preparation. In midwifery the lather may be superficially removed with a little water and the hands moistened with alcohol. The author reports a case in which he was compelled to perform version immediately without any preliminary preparation, and in which he washed his hands twice with afridol soap, after the second time allowing the soap to remain on the skin. Following this disinfection the puerperium ran an afebrile course. Peters recommends this soap as a non-irritating and effective antiseptic cleansing agent during childbirth.

Airol.

Satisfactory experiences with airol in the treatment of blenorrhœa neonatorum et adutorum in a period extending over ten years induced F. von Herrenschwand to

* Compare *Süddeutsche Apotheker-Zeitung* 1911, p. 248 and 534. Klotz, *Berliner klinische Wochenschrift* 1912, No. 2, p. 74.

** Compare Merck's Report 1910, p. 83.

Peters, *Münchener medizinische Wochenschrift* 1913, No. 30, p. 1694.

Herrenschwand, *Archiv für Ophthalmologie*, Vol. 82, No. 2.

investigate the bacteriological action of this preparation, and his results speak in favour of airol. The author found that the addition of only 0.01 per cent. of airol to the culture media completely inhibited the growth of gonococci. In addition, the bactericidal action of the preparation is considerably increased by the presence of sodium chloride and albuminous substances, which is probably not the case with most preparations of silver. In a concentration of 1:1,000 airol is capable of killing gonococci, while a 1:10,000 concentration appreciably diminishes the number of germs. In addition it possesses a pronounced penetrating action, which is apparent in the fact that the growth of gonococci in cultures is inhibited within a distance of 1.5 to 2 cm. from contact with the preparation, or to a depth of 0.5 cm. below it. Besides the desiccating effect of the bismuth* and the astringent action of gallic acid, the iodine present in airol, according to the author, is chiefly responsible for its property of killing gonococci. He was able to demonstrate experimentally that in addition to its action on gonococci airol also stimulates phagocytosis, in contradistinction to silver salts which exert a detrimental effect on phagocytosis. Therefore, the usefulness of airol in the treatment of blenorrhœa, as proved by its application in practice, has now been confirmed by experiment.

Frank reports a case in which bismuth was deposited in the cornea. He had treated the eye of a workman which had been injured by a blasting charge, with powdered airol and solution of mercuric chloride. After cleansing the wound of the cornea a 3 mm. broad zone of a brownish-black colour appeared on the cornea, which the author attributes to a deposit of metallic bismuth. He therefore urges caution when airol and mercuric chloride are employed simultaneously.

Alcohol.

The internal administration of alcohol and its value in infectious diseases is discussed in a very interesting work by C. A. Ewald on the basis of his own experience and of the data contained in the literature. Only the more important

* Airol is bismuth oxy-iodogallate.

Frank, *Wochenschrift für Therapie und Hygiene des Auges* 1913, No. 24, p. 193.

Ewald, *Medizinische Klinik* 1913, No. 31, p. 1233.

conclusions contained in his exhaustive work can be mentioned here, and are briefly summarized:

Alcohol cannot be employed as an antipyretic or bactericidal agent in acute or chronic infectious diseases in whatever doses it may be given. It does not impart to the blood any protective power, on the contrary, it rather diminishes the existing power, and it must be remembered in this connexion that alcoholics are also less resistant to infectious diseases than abstainers. Alcohol is of no use as a hypnotic. — Alcohol as an albumin-sparer is useless when administered once only, and its continued use is injurious. — In severe toxic or mechanical cardiac failure the stimulating effect of alcohol may prove useful. It certainly has the advantage of always being at hand and more quickly available for use than any other analeptic or stimulant. — As a stomachic, in cases where a direct action on the gastric mucous membrane is desired, the use of alcohol in acute and chronic infectious diseases can be entirely dispensed with, and it may be advantageously substituted by a suitable pepsine-hydrochloric acid mixture and a decoction of condurango, cinchona bark, etc. Although it apparently exerts a momentary favourable influence by reason of its psychical effect, it is not productive of any real and lasting benefit. — In the treatment of chronic infectious diseases, particularly in pulmonary tuberculosis, the author avoids the use of alcoholic beverages, as their use readily gives rise to gastric catarrh, and only impairs, instead of improving, the patient's state of nutrition.

W. Alexander and E. Unger advocate the treatment of severe trigeminal neuralgia by injections of alcohol into the Gasserian ganglion. In comparison with operative treatment, which is not always devoid of danger, treatment with alcohol presents decided advantages, even if relapses do occur in a number of cases. If it is possible to reckon upon freedom from recurrence during a few years surely this result may be described as satisfactory, especially as the renewed injection of alcohol again ensures a similar result. The authors give a detailed account of their technique, which cannot be briefly summarized. Treatment with injections of alcohol is particularly indicated in debilitated persons, in whom a resec-

tion might prove fatal. A. Loevy also adopted this method with a successful issue in a severe case; however, he considers this method of treatment to be indicated only in very severe cases, in which an operation might prove a dangerous procedure. The technique of injections of alcohol is discussed by F. Härtel, Alexander and J. Grinker. In one case D. Schwarz obtained a complete success by injecting 1 c. c. of alcohol (70 per cent.) according to Härtel's method. According to Flesch, deep injections of alcohol in genuine idiopathic tic douloureux are as effective as resection, in many instances even more so. Injections into the ganglion may prove beneficial even in the severest cases.

According to F. Hammer the treatment of skin diseases offers a wide field of application for alcohol. It may be used with advantage either per se, or in combination with corrosive sublimate, boric acid, wood vinegar, aluminium acetate, in the form of frictions, compresses, baths, etc. For these purposes ordinary commercial methylated spirit may be used, the odour of which may prove obnoxious but which is otherwise free from any injurious action. It has proved useful, inter alia, in hyperidrosis pedum, eczemas of the genital and anal regions, pruritus ani, oxyuris vermicularis, hæmorrhoids, vesiculosis manum et pedum, furunculosis, pemphigus, and burns.

B. Kozłowski reports upon the use of alcohol for the disinfection of the hands. He adopts the following method: After cleansing the hands for two minutes with soap and a brush which has been boiled, and drying with a sterile towel, they are scrubbed for three to five minutes with pledgets of cotton wool impregnated with alcohol, special attention being given to the finger-tips; the pledgets are frequently changed. After this procedure a pair of sterilized or boiled

Loevy, Berliner klinische Wochenschrift 1913, No. 17, p. 784.

Härtel, von Langenbecks Archiv für klinische Chirurgie, Vol. 100, No. 1. — Zentralblatt für Chirurgie 1913, No. 13, p. 493.

Alexander, Zeitschrift für physikalische und diätetische Therapie 1913, Vol. 17, No. 4.

Grinker, Journal of the American Medical Association, May 3, 1913.

Schwarz, Lijecnicki vijestnik 1913, No. 2. — Zentralblatt für Chirurgie 1913, No. 13, p. 492.

Flesch, Berliner klinische Wochenschrift 1913, No. 45, p. 2108.

Hammer, Württembergisches Medizinisches Korrespondenzblatt 1913; Zentralblatt für die gesamte Therapie 1913, No. 10, p. 535.

Kozłowski, Zentralblatt für Chirurgie 1913, No. 26, p. 1038.

Mikulicz's cotton gloves, impregnated with alcohol, and provided with long cuffs are put on, and during the operation they are frequently moistened with alcohol, or even changed. This procedure causes the skin of the hands to remain dry, hard and smooth, even during prolonged operations, or when several operations are performed in succession. The author never observed irritation of the skin to occur, nor was this produced on the gloves coming into contact with the tissues of the operation wound. E. Marquis is opposed to the use of soap as a preliminary to disinfection of the hands. His experiments show that it is sufficient to rub the hands well with pledgets of cotton wool moistened with alcohol 90 p. c. in order to render the skin almost entirely free from bacteria. On the other hand, it is not sufficient to moisten the hands with alcohol and then rub them together. After disinfection with alcohol the hands remain sterile for fifteen to twenty minutes.

For the disinfection of the hands, particularly in midwifery, H. Martius recommends an alcohol soap issued in the form of a paste under the name of "festalkol" and which contains 80 per cent. of alcohol*. Its antiseptic action is said to be equal to that of the best antiseptics for the hands, in addition to the fact that its practical use presents a number of advantages over other methods.

Aleudrin.

Further communications dealing with aleudrin** and its therapeutic uses have been published by E. Burchard, M. Wolfheim, Schlehan, Hirschberg and F. Johannessohn.

Burchard first tried the remedy on himself during an acute attack of gout. In addition to physical treatment, he took regularly doses of atophan and occasionally ten to fifteen

Marquis, *Revue de chirurgie* 1913, Vol. 32, No. 2.

Martius, *Deutsche medizinische Wochenschrift* 1913, No. 43, p. 2088.

* Compare Merck's Report 1910, p. 85.

** Compare Merck's Report 1912.

Burchard, *Deutsche medizinische Wochenschrift* 1913, No. 22, p. 1044.

Wolfheim, *Fortschritte der Medizin* 1913, No. 34, p. 933.

Schlehan, *Therapie der Gegenwart* 1913, No. 9, p. 431.

Hirschberg, *Psychiatrisch-neurologische Wochenschrift* 1913, No. 31.

Johannessohn, *Allgemeine medizinische Zentralzeitung* 1913, No. 29, p. 349.

drops of a 2 per cent. solution of morphine. He contented himself by taking relatively small doses of aleudrin, i. e., 0.5 gramme ($7\frac{1}{2}$ grains) three times a day, which displayed a satisfactory action on his subjective condition. The pains did not disappear entirely, but they became more bearable; a subjective feeling of well-being set in and sleep became quieter, without requiring the use of other hypnotics. Later the author made the same observations in his patients. By the use of larger doses — 1 gramme (15 grains) — he was able to effect the complete disappearance of pain. In purely neuralgic conditions, such as sciatica and trigeminal neuralgia, this analgesic action of aleudrin was displayed even more promptly and more effectively. The preparation also proved useful as a sedative and hypnotic in functional nervous conditions, particularly in anxiety neuroses (phrenocardia). In these cases a dose of 0.5 gramme ($7\frac{1}{2}$ grains), administered every three or four hours, produced a condition in which the patients evinced a certain indifference to their pains. Aleudrin further proved serviceable in chorea and whooping-cough in children. Hirschberg also obtained satisfactory results with the preparation in neurasthenic insomnia. Wolfheim was able to demonstrate that it displays a good hypnotic action even in tabetic pains, advanced degeneration of the cardiac muscle and their associated symptoms, occipital neuralgia, migraine coupled with climacteric troubles, etc.

Schlehan describes a case of tuberculosis of the lung and intestine coupled with severe gastric pains and insomnia in which doses of 0.02 gramme ($\frac{1}{3}$ grain) of morphine were powerless to relieve the pain or procure sleep, and in which doses of 1 to 1.5 grammes (15—24 grains) of aleudrin are said to have had the desired result. With equally satisfactory results the author was able to substitute the use of morphine by that of aleudrin in a severe case of asthma. He administered in the morning and afternoon 0.5 gramme ($7\frac{1}{2}$ grains) and shortly before going to bed 1 gramme (15 grains) of aleudrin, and later gradually decreased these doses. Sleep became normal and the attacks remained absent.

Johannessohn tried aleudrin in a woman who had undergone a colporrhaphia anterior et posterior and who suffered from pains in the loins. During the first four days he administered 0.5 gramme ($7\frac{1}{2}$ grains) four times a day, and then the same dose three times daily, with the result that the

pains disappeared completely. The author hopes to obtain successful results from the use of aleudrin as an adjuvant to anæsthesia.

A. Langgaard was able to demonstrate experimentally that aleudrin in fine crystals acts better than in coarse crystals.

A. Stob reports on the use of aleudrin in veterinary practice. His experience of its use in animals shows that the action of aleudrin in animals differs from that in man. He therefore comes to the conclusion that the use of the preparation as a narcotic and hypnotic for animals cannot be recommended since it is dangerous and its action is not reliable. It is best tolerated by dogs. From the author's statements it appears that the remedy acts all the more promptly the more highly developed the central nervous system is of the organism to which it is administered, as is also the case with morphine.

Allosan.

R. Hirsch has used allosan* only in those cases of gonorrhœa in which local treatment was temporarily contra-indicated. He gave 1 to 2 grammes (15—30 grains) three times daily, in cachets, or in tablets, and this medication was never objected to by the patients as the drug is tasteless and does not cause any gastric disturbances, nor does it affect the kidneys. In none of his cases was the author able to observe any extension of the gonorrhœal process to the posterior part of the urethra during the time that local treatment was suspended and allosan administered in its place. In six cases of gonorrhœal cystitis in which he gave the remedy the catarrh of the bladder was cured within 8 to 14 days without washing the bladder. In phimosis, and inflammation of the mucosa and prepuce, the purulent secretion diminished gradually in the course of a few days, and the number of gonococci present decreased appreciably. In nocturnal erections the administration of allosan allayed the pains to a minimum. Based on these satisfactory results, the author concludes that allosan is a very effective and non-irritant preparation of sandal-wood oil.

Langgaard, Berliner klinische Wochenschrift 1913, No. 44, p. 2044.
Stob, Dissertation Berlin (Tierärztliche Hochschule) 1913.

Hirsch, Klinisch-therapeutische Wochenschrift 1913, No. 14, p. 432.

* Compare Merck's Reports 1908—1912.

Almatein.

O. Fiertz deals exhaustively with the therapeutic uses and the value of almatein*, a preparation which has already been mentioned in these Reports. The author states that the antiseptic action of almatein was particularly apparent in intestinal affections such as colitis, enteritis, dysentery and typhoid fever, due to the fact that it is soluble in the alkaline intestinal juice. Its use is not to be recommended in gastric affections as it is insoluble in the acid gastric juices and is therefore incapable of displaying any antiseptic action.

Fiertz states that the field of application of almatein includes all forms of urticaria, and drug rashes such as have been observed after taking phenacetin and liquor ammonii anisati. To treat the urticaria present in a female patient with a tapeworm he prescribed 0.5 gramme ($7\frac{1}{2}$ grains) of almatein three times a day, with the result that the skin symptoms disappeared already on the second day. In other cases of urticaria he was able to obtain satisfactory results within the same time.

Mild forms of enteritis heal on an average within three days by using almatein, and the drug also displays a good effect in diarrhoea in tuberculosis.

Applied externally in the form of an ointment, almatein has proved useful in wounds, ulcers of the leg and in eczemas. Even infected wounds soon show an improvement and after applying a suitable dressing the secretion is considerably diminished. As the ointment does not irritate and is non-toxic it can be applied to burns. To alleviate the pain it is advisable to first apply naphtalan before making use of almatein, under the influence of which the wound soon assumes a better appearance. In the same way in the treatment of furuncles and phlegmons these should first be treated with lysol compresses or with a-chinosol ointment of the following composition: Chinosol 2.5 grammes (40 grains), Xeroform 10 grammes (150 grains), ung. zinci ad 100 grammes ($3\frac{1}{3}$ oz). Only when the symptoms of irritation in the wound have subsided should the almatein ointment be applied, the use of which stimulates the formation of granulations. It is also useful in ulcers

Fiertz, Korrespondenzblatt für Schweizer Ärzte 1913, No. 10; Deutsche Medizinal-Zeitung 1913, No. 17, p. 297.

* Compare Merck's Reports 1908—1912.

of the leg and in eczematous forms of the latter. Almatein is a useful preparation for the treatment of simple wounds and lacerations, and has the advantage that it never exerts an injurious action.

Aluminium Lactate.

For some years past greater interest has been shown in the therapeutic use of lactic acid*, and for this reason its salts also command more attention. A salt of lactic acid which up to the present had scarcely been used is aluminium lactate, now issued in the form of an aqueous solution. According to A. Perutz the 7 per cent. solution is a perfect substitute for the aluminium liquors, such as liquor aluminii aceticum and liquor aluminii acetotartarici, etc. This solution apparently keeps without decomposing; the author states that it remains clear for months; colonies of fungi may appear after it has been allowed to stand for some considerable time, these, however, may be removed by filtering, and their presence apparently does not affect the activity of the preparation. Perutz tested this preparation clinically for more than six months, using it in the same way as liquor aluminii aceticum.

In varicose ulcers of the leg Perutz applied moist compresses impregnated with 0.5—2 p. c. aluminium lactate solution. These were well borne and only sensitive patients complained of a transitory burning feeling. The action was satisfactory. On the other hand, the use of a 1 p. c. solution had to be abandoned in a patient suffering from ulcerated lupus of the face, as its application caused intense pain, whereas the same concentration of basic aluminium acetate solution caused scarcely any pain whatever.

In the care of the mouth in syphilitics undergoing mercurial treatment a 1 p. c. aluminium lactate solution renders the same service as a solution of basic aluminium acetate; it is well tolerated and readily used by the patients. In the treatment of eczema and skin affections aluminium lactate proved as useful as basic aluminium acetate.

Perutz also prescribed the use of aluminium lactate with satisfactory results in affections of the urethra and bladder, e. g., in post-gonorrhoeal catarrhs, in which it was used in

* Compare Merck's Reports 1910 and 1911.

Perutz, *Münchener medizinische Wochenschrift* 1913, No. 23, p. 1261.

a concentration of 1:1,000 to 1:500 in the form of irrigations. More concentrated solutions are liable to cause transient irritation. He was unable to establish any effect on the bacteria present, but this method of treatment certainly influenced the suppuration.

Alypin.

Impens discusses the question of the maximum dose of alypin in dealing with a case reported by Ritter in which the injection of 50 c.c. of a 2 p.c. solution of alypin into the field of operation to produce local anæsthesia was followed by toxic symptoms. He is of opinion that the dose employed in this case was too large, as it might easily give rise to dangerous toxic symptoms, especially in susceptible individuals. On the other hand, such large doses are not necessary, as a 0.5 to 1 p.c. solution is quite sufficient, especially if a preparation of the suprarenal gland is also used.

M. Steiner employed a 25 p.c. solution of alypin with highly satisfactory results as an anæsthetic in rhino-laryngological operations. Especially in resections of the lower turbinated bone it is said to have yielded excellent service, without causing toxic symptoms even when applied in large amounts.

J. Kieffer recommends the use of alypin tablets for producing anæsthesia in dental work. For simple extractions he dissolves one tablet (containing 0.02 gramme [$\frac{1}{3}$ grain] of alypin and 0.000065 gramme [$\frac{1}{1000}$ grain] of suprarenin) in 2 c.c. of normal saline solution; for extractions which promise to be difficult, or in teeth affected with periodontitis and for mandibular injections he dissolves the same dose in 1 c.c. The injection never failed to produce the desired result, when used either as a local anæsthetic or for conduction anæsthesia. Pain following the injection may be avoided by previously warming the alypin solution to body temperature, further by not injecting too quickly and by employing a properly sterilized syringe.

For particulars regarding the results of Schröder's in-

Impens, Medizinische Klinik 1913, No. 4, p. 138.

Ritter, Medizinische Klinik 1912, No. 30, p. 1236.

Steiner, Klinisch-therapeutische Wochenschrift 1913, No. 31, p. 917.

Kieffer, Deutsche zahnärztliche Wochenschrift 1913, No. 18.

Schröder, Deutsche medizinische Wochenschrift 1913, No. 30, p. 1459.

vestigations on the toxicology of alypin by means of experiments on animals, the original paper should be consulted; mention may also be made of a review of the literature of alypin by Seifert.

Ammoniated Citro-Arsenite of Iron.

I supply under this designation a preparation of iron in scales, which corresponds to a content of 15 to 18 p. c. of iron and 1.4 per cent. of arsenious acid. It is soluble in water and has been used with successful results, given by mouth and especially subcutaneously or by intragluteal injection, in anæmias, chlorosis, scrofula, conditions of debility and pellagra*. The usual dose, given every second or third day, is 0.035 to 0.075 gramme ($\frac{1}{2}$ — $\frac{1}{6}$ grain) in 1 c. c. of water.

S. Kowler again draws attention to the value of this preparation in secondary anæmias, and the results of his investigations show that ammoniated citro-arsenite of iron is a drug which deserves full consideration. Of particular interest are his reports dealing with the treatment of secondary anæmias with defibrinated blood and this preparation of iron. The injections of blood were given intramuscularly, and contributed markedly towards effecting an improvement. Defibrinated human blood in doses of 15 to 20 c. c. was used. The iron solution is more easily obtained. Kowler dissolved 0.5 gramme ($\frac{7}{12}$ grains) of ammoniated citro-arsenite of iron in 10 c. c. ($\frac{1}{3}$ oz) of sterile water**, and this solution was injected in doses of 1 c. c. (17 min.) twice a week, at first intramuscularly and later subcutaneously. He found that subcutaneous injections are less painful than intramuscular injections, and for this reason he prefers the former method. The effect of the injections was manifest in a considerable increase in the number of red blood corpuscles and in the hæmoglobin content, and also in an improvement in the general condition. It may be mentioned in this connexion that a course of dietetic-hygienic treatment, alone or combined

Seifert, Würzburger Abhandlungen 1913, Supplementheft.

* Compare Merck's Report 1899, p. 74, 1900, p. 100 and 1911 p. 147.

Kowler, Dissertation Jena 1912.

** For this purpose I supply the preparation in doses of 0.5 gramme ($\frac{7}{12}$ grains), in sealed ampoules.

with iron and arsenic pills, was not capable of effecting an equally good result; he even found that with suitable feeding neither the number of blood corpuscles nor the hæmoglobin content showed an increase.

Anæsthesine.

H. Rosenhaupt has prescribed anæsthesine for several years with very good results in nervous vomiting in children. He administered it in a 2—3 p.c. mucilaginous mixture, a teaspoonful of which is given about ten minutes before meals. The remedy displays a prompt effect in reflex disturbances of deglutition such as are frequently observed in slight lesions of the upper part of the alimentary canal. The author was unable to obtain any definite successes from its use in cases of pylorospasm of the Hirschsprung type, which exhibit the following leading symptoms: occurrence before the eighth week, constipation, wasting and considerable contraction of the stomach, frequently accompanied by the formation of a tumour-like swelling, and aversion to liquids, which is a prominent symptom in these cases. However, since it is often very difficult for the practitioner to distinguish between a case of simple pylorospasm from one of the Hirschsprung type, Rosenhaupt states that anæsthesine may to some extent serve as a means of making a differential diagnosis. He was also able to establish that it may be used to differentiate between vomiting of cerebral origin and local vomiting from gastric causes. Also in cases where there is a suspicion of tuberculous meningitis a test may be made by anæsthetising the stomach to establish the etiology of the vomiting.

M. Kärcher found anæsthesine a useful remedy in the gastric pains caused by achylia. He also obtained remarkable symptomatic successes in the troubles due to hyperchlorhydria. In addition to etiological treatment he administered 0.5 gramme ($7\frac{1}{2}$ grains) of anæsthesine in a cachet. The remedy also yielded good results in several cases of nervous dyspepsia, vomiting of pregnancy, and vomitus matutinus potatoris. For the symptomatic treatment of acute and chronic "cold" the author found the following ointment extremely useful: An-

Rosenhaupt, Deutsche medizinische Wochenschrift 1913, No. 16, p. 752.

Kärcher, Therapie der Gegenwart 1913, No. 8, p. 382.

æsthesine 1 gramme (15 grains), ung. boric. cereat. ad 20 grammes ($\frac{2}{3}$ oz); in some cases the author prescribed the addition of 0.2 gramme (3 grains) of soziodol-sodium. He does not think it necessary to add menthol, nor is he convinced of the curative effect of the latter; on the contrary, he believes that it has an irritant action. By the use of the ointment mentioned above he was able to abort the severest "cold" and its application immediately relieved the pain and irritation, while the nasal secretion disappeared almost as rapidly. In children, particularly in the catarrhal symptoms in measles, the use of the ointment containing the addition of soziodol is worthy of consideration. As it allays the irritation the children cease to scratch and the catarrh is quickly cured; its use apparently prevents middle-ear complications.

Antiformin.

According to J. Ritzer antiformin* is an extremely useful preparation for the treatment of nodular glanders, particularly in view of the fact that it dissolves mucus and consequently is capable of exerting a deep action on mucous membranes. Further, it dissolves bacteria and therefore displays a bactericidal action in addition to softening fæces and for this reason is especially suited for the disinfection of stables. While making use of antiformin in the treatment of foot and mouth disease the author made the observation that in animals affected with nodular glanders the lymph-follicles lost colour and shrunk in a remarkable manner; these appearances were undoubtedly due to the action of antiformin. Further trials showed that antiformin is extremely useful in these cases since it yielded very good results in cases in which bacillol proved ineffective. Ritzer recommends the following method:

All the animals are thoroughly disinfected once a week with a 3 p.c. solution of antiformin, applied by means of a garden syringe, special attention being paid to the disinfection of the vaginal region; the brushes, stable and stable utensils also being disinfected with this solution. Care should be taken to spray the solution well on to the bodies of the

Ritzer, Berliner tierärztliche Wochenschrift 1913, No. 24, p. 437.
(Compare also Münchener tierärztliche Wochenschrift 1912, No. 1.)

* Compare Merck's Reports 1908—1910.

animals and also about the stable. In female animals the rima vulvæ is opened so as to permit of thoroughly spraying the posterior parts of the vagina. The animals bear this treatment very well, at the most the impregnation of the air with antiformin causes animals affected with pulmonary disease to cough. In the intervals between the weekly disinfection two capsules of antiformin ointment (10 p.c.) are introduced into the vagina.

M. Merres tried antiformin in mange in dogs, but in spite of using a 10 per cent. solution for weeks he was unable to observe any healing effect.

Antimony Pentachloride (Antimonii Perchloridum).

Antimony perchloride, SbCl_5 , is a yellow liquid which emits fumes on coming into contact with the air. It is soluble in a small amount of water; in the presence of a large quantity of water it is decomposed into antimony pentoxide and hydrochloric acid. It is miscible with carbon tetrachloride.

According to S. Hilpert and L. Wolf antimony pentachloride may be used as a test in the analysis of aromatic hydrocarbons. For this purpose about 0.1 gramme of the hydrocarbon to be tested is dissolved in 1—2 c.c. of carbon tetrachloride, and to this mixture is added drop by drop a mixture of one part by volume of antimony pentachloride and two parts by volume of carbon tetrachloride. Pure benzol produces a yellow to reddish-yellow colour, while commercial benzol containing thiophen gives rise to a dirty green coloration soon leading to a dark coloured precipitate. If 1 c.c. of benzol is used for the test the presence of 3 milligrammes of thiophen causes within a few seconds the production of a greenish-brown cloudiness. Carbazol produces a different colour — green — which can be used to distinguish it from thiophen.

Hydrocarbons with condensed benzol rings yield darker shades of colours. Thus dilute solutions of naphthalene produce a yellowish-brown colour and within a few seconds a lilac coloured precipitate; solutions of indene yield a dark red precipitate with a bluish tinge; anthracene a green, and anthraquinone a vermilion precipitate.

Merres, Dissertation, Hanover, 1913.

Hilpert - Wolf, Berichte der deutschen chemischen Gesellschaft, Berlin 1913, Vol. 46, p. 2215.

Methylated hydrocarbons produce a coloration ranging from red to lilac. Toluol, the xylols, mesitylen and cumol produce a red coloration which increases in intensity with the number of methyl groups. Chlorine substitution products of hydrocarbons in the ring show only a slight difference in colour as compared with the corresponding non-substituted hydrocarbons, while substitution with the nitro, amino and carboxyl groups produces lighter shades.

Antimony, Preparations of

The successes obtained with atoxyl and arsacetin in the treatment of diseases caused by trypanosomes and spirochætes were instrumental in substituting the use of preparations of arsenic by that of preparations of antimony, as the latter may be regarded as less toxic than the former. The first experiments in this direction undertaken with tartar emetic (antimonyl potassium tartrate)* were apparently not quite satisfactory. During the past year a large number of organic compounds of antimony were tried, and a few of these were recommended for further therapeutic investigation. P. Uhlenhuth, P. Mulzer and G. Hügel have investigated the chemotherapeutic properties of the following two preparations:

1. Benzolsulphone-para-aminophenylstibine sodium. This preparation, the composition of which is analogous to that of hectine**, contains 26 p.c. Sb; it possesses a considerable prophylactic and curative action against fowl spirillosis, if injected in amounts (0.2 gramme) approaching the toxic dose. The authors' experiments, however, show that smaller doses (0.1 gramme) may exhibit a protective and curative effect in fowls. The preparation is readily soluble in water with an alkaline reaction. The solutions, however, do not keep well.

2. Para-urethanophenylstibine sodium (32 p.c. Sb), is still more efficacious and appears to be somewhat less toxic. A dose of 0.2 gramme was always well borne, which was not always the case with benzolsulphone-p-aminophenyl stibine sodium. On the other hand, the curative dose

* Compare Merck's Reports 1908, p. 334 and 1911, p. 433. Uhlenhuth-Mulzer-Hügel, Deutsche medizinische Wochenschrift 1913, No. 9, p. 393.

** Hectine is sodium benzo-sulpho-p-aminophenylarsinate. Compare Merck's Report 1909, p. 226.

of para-urethanophenyl stibine sodium was somewhat smaller, as a dose of 0.2 gramme proved very effective. The aqueous, neutral solution of this compound is not stable.

3. Acetyl-para-aminophenyl stibine sodium. This preparation, the composition of which is analogous to that of arsacetin*, was found to be less effective in fowl spirillosis than the other two preparations. The curative dose is about 0.5 gramme per kilogramme of fowl, the lethal dose is about 1 gramme.

4. Para-aminophenyl stibine sodium, the chemical composition of which corresponds with that of atoxyl**, is more poisonous than the foregoing. A single dose of 0.1 gramme usually causes the death of the fowls. 0.05 gramme is the amount which is generally well tolerated. However, it failed to exhibit either a curative or prophylactic effect in fowl spirillosis.

The following substances were found to be useless, or displayed only a very slight action:

Phenyl stibine sodium,

Acetyl-meta-aminophenyl stibine sodium,

Acetyl-para-aminophenyl stibine mercury,

Meta-amino-para-chlorophenyl stibine oxide and its acetyl derivative,

Meta-amino-para-chlorophenyl stibine sodium,

Meta-amino-para-oxyphenyl stibine sodium and the dye produced from it with β -naphthol,

Acetyl-meta-amino-para-oxyphenyl stibine sodium,

Meta-amino-stibiobenzol and its acetyl derivative,

p. p'-dioxy-m.m'-diaminostibiobenzol and its acetyl derivative as well as its compound with salicylaldehyde,

Meta-aminophenylstibinic acid,

Meta-aminophenyl stibine hydrochloride.

The authors also made experiments with the preparations described above under 1, 2 and 3 in rabbit syphilis and in animals infected with the spirilla of relapsing fever, dourine and trypanosomes. The results obtained were in part satisfactory, particularly in scrotal syphilis in rabbits. The sub-

* Arsacetin is sodium acetylaminophenylarsinate. Compare Merck's Report 1908, p. 132.

** Atoxyl is sodium para-aminophenylarsinate. Compare Merck's Report 1907, p. 36.

cutaneous injection of acetyl-para-aminophenyl stibine sodium in a few cases of human syphilis was accompanied by pain and irritation, although a therapeutic effect was evident.

In order to definitely establish the value of preparations of antimony, particularly in infections due to trypanosomes, W. Kolle, O. Hartoch, M. Rothermundt and W. Schürmann undertook systematic investigations which yielded the following results: A single intramuscular injection of metallic antimony or of various insoluble organic as well as inorganic compounds of antimony is capable of healing trypanosome infection in mice with certainty, provided a compound of antimony is used in which the antimony is present in trivalent form. The mice, however, die from chronic poisoning, but are sterile. However, trivalent compounds of antimony are known which are relatively very slightly toxic on intramuscular injection, as for instance antimonious oxide (Sb_2O_3), and the name "trixidin" was applied by the authors to a 30 p. c. oily emulsion of this compound. Of all the known preparations of antimony this is the most active on intramuscular injection, taking into consideration the chemotherapeutic index and its lasting sterilising effect, while it does not give rise to acute or chronic poisoning. One or two intramuscular injections of absolutely non-toxic doses of trixidin effect the permanent sterilisation of animals infected with trypanosomes in 100 p. c. of the cases treated. As regards its index (1:100), trixidin stands far above all other preparations of antimony, indeed it surpasses all the hitherto known insoluble chemotherapeutic remedies. The question of tolerance to antimony is for this reason largely deprived of its importance in the chronic treatment of trypanosome infections in man and in the larger animals. Preparations of antimony which are insoluble in water, including metallic antimony, act with almost the same rapidity as the water-soluble poisonous compounds, such as tartar emetic. The pentavalent compounds of antimony are devoid of almost any pharmacological or therapeutic action. If they have any action at all, this is only apparent on using doses which closely approach the lethal dose.

Kolle and his collaborators include the following among the active preparations capable of practical employment: Tartar

emetic, dimethylphenylpyrazolone sulphamino-antimony trichloride, dimethylphenylpyrazolone acetyl antimony trichloride, dimethylphenylpyrazolone acetyl antimony trichloride ointment, antimony ointment (prepared with metallic antimony), and trixidin; on the other hand, they admit that antimony in small repeated doses, antimony-potassium fluoride and chloro-antimony ointment are effective, but useless for practical purposes.

Special importance attaches to the use of insoluble preparations of antimony in ointment form, for the reason that these are effective and at the same time non-injurious, even if their intramuscular injection causes toxic symptoms. The experiments of the authors cited above have shown that the use of these ointments for inunction in the treatment of acute and chronic trypanosome infections in small animals, such as mice, rats, guinea-pigs, rabbits and monkeys, is capable of effecting a cure without recurrences in 66 p.c. of the cases treated, without the occurrence of the slightest toxic secondary effects.

Antiluetin is a preparation described by M. Tsuzuki. According to his statements it is bitartrato-potassium-ammonium-antimony oxide, of the chemical formula $\text{SbO}(\text{C}_4\text{H}_4\text{O}_6)_2\text{K}(\text{NH}_4)_2 \cdot \text{H}_2\text{O}$, its composition therefore corresponds to one molecule of tartar emetic and one molecule of ammonium tartrate ($\text{SbO} \cdot \text{C}_4\text{H}_4\text{O}_6 \cdot \text{K} + (\text{NH}_4)_2\text{C}_4\text{H}_4\text{O}_6$). It is described as a substance the organotropic properties of which are diminished while its parasitotropic properties appear increased, the latter would be due to the introduction of ammonium tartrate into the antimonyl potassium tartrate molecule. The theoretical speculations of the author cannot be entered into here, and only his practical experiences will be briefly reproduced, based on the statements published by the author himself and his collaborators, K. Ichibagase, H. Hagashi and Htana. After the preparation had been used with success in scrotal syphilis of rabbits, the above mentioned authors undertook its trial in man. Antiluetin was prescribed in the following combination:

Rp. Antiluetin	2.5 grammes (40 grains)
Cocain. hydrochlor.	2.5 „ (40 „)
Aq. dest.	100 „ (3 1/3 oz)
M. Sig.:	1—2 c.c. for subcutaneous injection.

Tsuzuki, Ichibagase, Hagashi, Htana, Deutsche medizinische Wochenschrift 1913, No. 21, p. 985 and 988.

In addition to these injections it is advisable to employ other reliable antisyphilitic remedies internally or externally, such as preparations of iodine and mercury. For this reason the authors usually first submitted their patients for some time to treatment with iodine and mercury, and then proceeded to make use of antiluëtin. They were satisfied with the results obtained by this method. They fixed the dosis sterilisans magna of antiluëtin for man at 0.75 gramme (12 grains). It is best to begin with doses of 0.025 gramme ($\frac{2}{5}$ grain), injected with aseptic precautions between the scapulæ. The dose is then increased to 0.05 gramme ($\frac{3}{4}$ grain), and the remainder is administered in small amounts in the course of the following four or five days, until a total amount of 0.15 or 0.3 gramme ($2\frac{1}{3}$ —5 grains) has been reached. If the injections are well borne they are continued, and it is possible to give daily doses up to 0.1 gramme ($1\frac{1}{2}$ grains) of antiluëtin. Should local reactions, to which the authors allude without entering into details, necessitate caution, then treatment should be begun with diluted solutions.

P. Dubois makes a statement which is worthy of note, to the effect that the action of arsenophenylglycin in experimental syphilis in rabbits may be increased by the simultaneous use of tartar emetic. This combined treatment caused the disappearance of the spirochætes after three to six days, and the inoculation chancre cicatrised completely within two to three weeks.

Aperitol.

K. Rühl has employed aperitol* for four years in his practice and reports his observations. In addition to patients suffering from disturbances of digestion, gastric and intestinal disorders and chronic obstipation, he used it also largely in cases of skin diseases associated with disturbances of digestion, or in which the latter might safely be assumed to be the cause of the former. Urticaria, acne vulgaris, eczemas and gonorrhœal affections preponderate among these cases, in which a regular action of the bowels appears indicated as an adjuvant to the treatment adopted.

Dubois, Zeitschrift für Chemotherapie 1912, Vol. 1, p. 203. — La Polyclinique 1913, Vol. 22, p. 181.

Rühl, Klinisch-therapeutische Wochenschrift 1913, No. 24, p. 719.

* Compare Merck's Reports 1908—1912.

Aperitol was administered to children and adults in the form of tablets or bonbons, each containing 0.2 gramme (3 grains) of aperitol. It was generally given in the evening before going to bed; in some instances it was given in the morning, according to the patient's age, in doses of one to four tablets. The author lays stress upon the fact that with this treatment he never observed any undesirable secondary effects or unwelcome sequelæ. After seven to fourteen hours painless evacuation took place; the motions were pultaceous or semi-solid. The drug proved effective in practically every case; in a few cases, however, the dose had to be increased to three or four tablets to produce the desired effect, and sometimes it took longer to act, although its action always set in after some time. In no case was tolerance to the remedy established, on the contrary, its action remained uniformly good. A further valuable property of aperitol, according to Rühl, is the absence of the feeling of lassitude which is so frequently observed to follow evacuation of the bowels as a sequel to the use of most purgatives. The author obtained excellent results with the drug in several cases of urticaria, as in these it displays a sedative action in addition to its effect of cleansing the bowels. In these cases, however, in order to obtain a more intense action larger doses are required, and usually three to four tablets were given on the first day, and two to three tablets on the second day.

Apomorphine.

In a monograph on the pharmacological action of apomorphine M. Feinberg deals with the question whether the formation of apomorphine is likely to take place on boiling solutions of morphine, as several authors formerly maintained to be the case, and recently Overlach has drawn attention to this possibility. The definite solution of this question is a matter of general interest since it has been suggested that the vomiting sometimes observed after injections of sterilized solutions of morphine may be due to the formation of apomorphine from the morphine during sterilisation. The exhaustive investigations of the author prove that no formation of apomorphine takes place even on boiling

solutions of morphine, or liquids containing morphine, for a considerable time, nor does this occur with solutions of this kind after standing for a prolonged period, even if they contain nutrient fluids*. Therefore, statements to the effect that solutions of morphine, or liquids containing morphine, may be contaminated by the presence of apomorphine should be deleted from the text-books.

In the course of his investigations, Feinberg discovered two tests for apomorphine, one of which deserves special consideration from the fact that it permits the demonstration of apomorphine in the presence of morphine, and is not influenced by morphine. It is applied as follows: If apomorphine hydrochloride be dissolved in a large quantity of water and 3 drops of a 1 per cent. solution of potassium ferricyanide be added, on the addition of 1 c. c. of benzol, the latter, on shaking, assumes an amethyst-red colour. On adding a few drops of dilute solution of sodium carbonate and again shaking, the colour of the benzol layer turns to violet-red, which on standing for some time changes into a beautiful violet colour. In the presence of free acid the reaction is almost completely absent. This test is extremely sensitive as it will show the presence of 0.000003 gramme of apomorphine in 1 c. c. of solution, and by the addition of sodium carbonate it is made still more delicate. Morphine and other opium alkaloids do not give this reaction, nor do they influence its sensitiveness as a means of detecting the presence of apomorphine.

Aponal.

According to Ollendorf aponal** exerts a mild hypnotic action in cases of insomnia due to over-excitement of the central nervous system, whether as an accompanying symptom of neurasthenia or of other bodily affections, such as heart disease, lung disease or rheumatic affections. The usual dose is 1 to 1.5 grammes (15 to 24 grains), three times a day, and only in a few cases a dose of 2 grammes (30 grains) is required, nor does the author recommend the use of larger doses. With this dosage he never observed

* Nor is chloromorphide formed.

Ollendorf, Allgemeine medizinische Zentralzeitung 1913, No. 30, p. 359.

** Compare Merck's Reports 1911—1912.

any undesirable secondary effects; gastro-intestinal troubles and irritation of the kidneys never occurred. In psychoses, as long as they were not accompanied by extreme excitement, he was able to observe a marked sedative effect after the systematic administration of small doses. He therefore advocates the administration of 0.25 to 0.5 gramme (4—7½ grains) of aponal three times daily for several weeks, and in most cases he obtained good results with this treatment. The patients became calmer, sexual excitation diminished, and the patients showed a more equable frame of mind. Stuart Hallows has also used aponal with satisfactory results in simple insomnia, but he states that it is not suitable for sleeplessness due to pain. The drug has proved particularly useful in dementia præcox.

Herzberg recommends the use of aponal not only to combat simple insomnia, but also as an analgesic and hypnotic after operations. After a dose of 2 grammes (30 grains) sleep was induced within half an hour to one hour and a half, which lasted for six to seven hours. The patients' condition on the following day was usually good, and no after-effect was apparent, at the most there was a slight feeling of lassitude. Herzberg administered aponal in powder or tablet form in a large amount of warm tea.

Z. Wachtel's statements regarding the value of aponal agree with those of the above mentioned authors.

Argulan.

Argulan, according to W. Kolle and Rothermundt, is antipyrine sulphamino-mercury, a white crystalline powder, insoluble in water, containing 46.8 per cent. of mercury. The authors have not as yet published any details regarding the chemical structure of this compound. The pharmacological investigations undertaken with this preparation have shown that it displays a comparatively rapid action in fowl spirillosis and in experimental syphilis; its parasitotropic effect is particularly marked, and it almost equals salvarsan as regards freedom from recurrences. These findings were to a large extent

Hallows, Medical Press and Circular, June 4, 1913.

Herzberg, Fortschritte der Medizin 1913, No. 16, p. 427.

Wachtel, Przegląd lekarski 1912, No. 19.

Kolle-Rothermundt, Medizinische Klinik 1913, No. 21, p. 835.

confirmed when using the drug in syphilitic patients. Argulan was tried by a number of doctors principally in early syphilis with primary manifestations, secondary exanthemata and also in tertiary syphilis, and as far as can be inferred from the results so far obtained, it displays a uniform powerful action in all stages of syphilis; its effect is especially manifest on primary symptoms and primary enlargement of the glands. The author states that even syphilides which are apparently relatively resistant to mercury may be influenced by the use of larger doses (6 to 8 injections of 0.3 c. c. of a 40 per cent. emulsion). The fact that experiments on animals showed that it is only slightly organotropic, and is therefore apparently less injurious than calomel or salicylate of mercury, makes the use of larger doses appear permissible. This is also borne out by the observation that repeated injections of as much as 0.75 c. c. of the 40 per cent. emulsion of argulan were well tolerated.

R. Stanziale gives fuller details regarding the use of argulan. He states that the rather viscid 40 per cent. emulsion of argulan should be stirred with a sterile glass rod prior to its use, warmed on the water-bath and injected by means of a Pravaz syringe with a wide bore. The author gave as an initial dose 0.1 c. c. of the emulsion, corresponding to 0.019 gramme of mercury. If this amount was tolerated he increased the dose to 0.4—0.5 c. c. The second injection was given three or four days after the first, and then the intervals between the injections were gradually increased up to a fortnight. The larger doses caused transient pain and swelling, and in some cases led to abscess formation. General reactions, such as increase of temperature and stomatitis, were also observed; on the other hand, symptoms of mercurial intoxication never occurred. Stanziale also reports two cases of malignant syphilis in which argulan rendered good services, and he mentions that it displayed a favourable effect on the lightning pains of tabes.

Arsacetin.

In a case of spindle-celled sarcoma of the ovary, which showed a recurrence in the course of a year after extir-

pation, L. Seeligmann obtained a successful result with arsacetin which encourages further trials with his method. The recurrence had already involved the spine, and on opening the stomach was found to be inoperable, as the tumour had developed retroperitoneally and starting from the lymphatic glands of the small pelvis extended to a level with the twelfth dorsal vertebra. As the general condition of the patient showed an improvement after the operation wound had healed, and in view of the desperate nature of the case, the author decided to try intravenous injections of arsacetin, particularly as Sick had six years previously obtained transient satisfactory results with subcutaneous injections of atoxyl in some cases of osteosarcoma. In addition to X ray treatment of the tumour, he administered 0.1 gramme ($1\frac{1}{2}$ grains) of arsacetin four times a week, and after an interval of four weeks again gave an intravenous injection of 0.1 gramme ($1\frac{1}{2}$ grains) of arsacetin. The injections were well borne, only after the second injection rigor and a considerable rise in temperature (39.5° C.), occurred, which, however, fell to normal on the following day. The result of this combined treatment was most striking. The tumour decreased constantly in size, the patient's weight increased and her general health improved to such an extent that she was able to leave her bed after five weeks and regained a healthy colour. A radiographic examination showed that the metastatic process in the spine involved the twelfth dorsal vertebra and the first lumbar vertebra, and the author believes that it shows a prospect of healing. The large tumour can no longer be felt, and the pains have disappeared. Possibly this method of treatment is in principle capable of yielding good service, at least in inoperable recurrences in cancerous tumours.

Arsenical Paste, Zeller's

R. Eben obtained a very satisfactory result in an ulcer caused by X rays, which had persisted for eleven months. The case was that of an employé in an institution who had for a long time worked an X ray apparatus without any protection, and had contracted a painful tumour at the terminal

Seeligmann, Münchener medizinische Wochenschrift 1913, No. 12, p. 637.

Eben, Prager Medizinische Wochenschrift 1913, No. 36.

phalanx of one thumb. The tumour was diagnosticated histologically as X ray carcinoma and demanded operative treatment. In addition, an X ray ulcer had developed on the index finger of the other hand, which after several months had become 2 cm. long and $1\frac{1}{2}$ cm. broad. As an operation was declined, the author gave the patient three times a day 15 drops of solution of sodium silicate and applied arsenical paste under a suitable dressing; the paste consisted of 2.5 grammes (40 grains) of arsenious acid, 7.5 grammes (112 grains) of red mercuric sulphide and 4 grammes (60 grains) of animal charcoal*. After the size of the tumour had increased somewhat, he applied airol gauze, and irrigated the tumour with 3 per cent. perhydrol solution. Under this treatment the necrotic tissues were cast off, and after a further period of three weeks epithelization of the tumour was completed. Silicic acid was administered to the patient for a period of three months. Eben does not attribute the successful issue to the internal medication, but solely to the caustic action of the modified Zeller's paste.

S. von Stein also employed Zeller's arsenical paste with a successful result, in combination with the administration of nakasilicium, and after five months' use succeeded in healing a carcinoma of the lip. He advocates this method particularly in external, readily accessible carcinomata in the initial stage, where it may possibly obviate an operation.

Arsentriferrin.

Arsentriferrin**, according to F. Gehring, is an iron preparation which answers all requirements as regards freedom from any undesirable effects on the stomach and satisfactory absorption, and for these reasons its clinical test has yielded good results. The author prescribed the preparation in over twenty cases and was able to observe in every case an increase in the hæmoglobin content of the blood, while the patients showed a corresponding increase in weight. Headache and vertigo, if present, frequently disappeared within a very short time under this treatment. Hence, arsentriferrin has

* Compare Merck's Report 1912, p. 406.

Stein, Jeshemesjatschnik Uschnych, Gorlowych i Nosowych Bolesnej 1913, Vol. 8, p. 398.

** Compare Merck's Report 1910.

Gehring, Fortschritte der Medizin 1913, No. 31, p. 847.

shown itself to be a remedy capable of rendering good service in the treatment of anæmias and conditions of debility. In a few cases of dysmenorrhœa and amenorrhœa the author was also able to effect an improvement or a cure by its use. The preparation was always well borne, even in cases of gastro-enteritis and gastralgia, and only in exceptional cases in females slight constipation was observed at the commencement of treatment. It is advisable to begin treatment by administering one tablet three times a day, half an hour after meals; the tablets should be well chewed. After ten to fourteen days the dose is doubled for a period of five to six weeks; in some cases during the last week of treatment the initial dose of one tablet three times a day may be resumed. It is also possible to administer one tablet morning and evening and two tablets at midday throughout the whole treatment.

K. Jochem also obtained good results with arsentriferrin in the treatment of anæmia, chlorosis, scrofula, deficient nutrition, nervous conditions of exhaustion and weakness, and affections on a tuberculous basis. He prescribed for adults two tablets three times a day, and for children one tablet three times daily, to be taken after meals, and forbade the use of fruit and spices. With this treatment the appetite and the general condition improved within a short time. In the after-treatment of convalescence from whooping-cough arsentriferrin also proved of use.

R. Gelhausen speaks highly of the value of arsentriferrin in anæmia, chlorosis, neurasthenia and hysteria associated with poor nutrition. Only in three cases the patients complained of a feeling of fulness and pressure in the abdomen at the beginning of the treatment, or pains in the stomach or nausea were observed. In these cases Gelhausen caused the tablets to be powdered and mixed with the food, with the result that the unwelcome effects disappeared.

Arsentriferrin.

A very favourable opinion of arsentriferrin* is expressed by C. A. Ewald, who submitted this preparation to an

Jochem, *Ärztliche Mitteilungen* 1912, No. 50.

Gelhausen, *Halbmonatsschrift für soziale Hygiene* 1913, No. 1.

* Compare Merck's Reports 1908 and 1911.

Ewald, *Medizinische Klinik* 1913, No. 3, p. 94.

exhaustive clinical trial in 46 cases. He paid particular attention to the effect produced by the preparation in well defined gastro-intestinal affections, and especially in gastric ulcer. The cases treated by him include ulcers of the stomach and duodenum, achylia gastrica, cancer of the stomach, severe hæmorrhoidal hæmorrhage associated with anæmia, anæmia, chlorosis, and gastric crises of tabes. The author comes to the conclusion that arsentriferrol is a preparation which may be administered without fear even in ulcers of the stomach and duodenum. Among 28 cases its use had to be abandoned owing to pains in the stomach in only two cases. In four cases of achylia gastrica it was tolerated without inconvenience and the hæmoglobin content showed an increase of 5—25 per cent. In cancer of the stomach an increase in the hæmoglobin content was also observed, as well as an increase in the blood corpuscles and body-weight, although the nature of the cases precluded from the beginning any hope of a success. In other cases of cancer, however, failures were observed, but in view of the fact that the author purposely employed this treatment in patients with pronounced anæmia, the severity of the affection and particularly of the anæmia must be taken into consideration in forming an opinion regarding the results. Nevertheless, the use of arsentriferrol may prove expedient in cases which will probably undergo operation later on, as a general improvement of the patient's strength beforehand can only prove favourable.

Treatment with arsentriferrol led to a considerable increase in the hæmoglobin content in a patient suffering from profuse hæmorrhoidal hæmorrhage, in a case of anæmia of doubtful origin (probably chlorotic), and in the gastric crises of tabes. On the whole, Ewald gained the impression that the patients who were given arsentriferrol improved more rapidly and felt better than those who did not receive this treatment.

E. Hartung also employed arsentriferrol with good results in a number of cases of anæmia. He was able to confirm the tolerance of the preparation in cases associated with cancer of the stomach. In a syphilitic in the secondary stage he was able to observe a decrease in the anæmia and in the headaches after administering the preparation for three

weeks. In hysteria and neurasthenia the use of this remedy also yielded good results. Arsentriferrol is particularly useful in chlorosis, in which iron is generally not well borne, whereas this preparation is readily tolerated.

Aspirin.

The ready solubility in water of "aspirin soluble"* is, according to Hebestreit, a distinct advantage over aspirin, inasmuch as it is not necessary to administer this preparation in tablet form. Since it is almost tasteless it may be given in a mixture of the following composition:

Aspirin solubil.	8 gramme (120 grains)
Aq. dest.	175 „ (6 oz)
Syr. Rubi Idæi	ad 200 „ (7 oz)

Of this mixture adults are given one tablespoonful three to four times a day; to children correspondingly smaller doses are given, e. g., one teaspoonful to one dessertspoonful three to four times daily. It must be borne in mind, however, that solutions of soluble aspirin do not keep well and after a few days the preparation splits off acetic acid. For this reason the amount of the mixture prescribed should be sufficient to last for not more than a few days. In addition to its great solubility the compound, according to Hebestreit, possesses the advantage of being a neutral combination, a point which is of importance when administering it to patients suffering from gastric complaints associated with increased production of acid. The calcium component may also possess a certain value as it contributes to maintain the action of the heart and displays a slight sedative effect.

The experience of this author with aspirin soluble extends principally to its use and tolerance in neurasthenia, particularly in accident neuroses. He administered to adults at first a dose of 0.5 gramme ($7\frac{1}{2}$ grains), and repeated this dose after one hour, if necessary. In most cases the action was satisfactory and resembled that of aspirin. The preparation was usually well borne and only occasionally a patient complained of palpitations, a symptom which has also been observed after aspirin.

Hebestreit, Allgemeine medizinische Wochenschrift 1913, No. 38, p. 449.

* Compare Merck's Report 1912.

Asurol.

Asurol, which has already been discussed in these Reports*, was found by Ijiri to be a useful antisyphilitic. A weekly injection of 3 c.c. of the 5 p.c. solution was sufficient to effect a decrease in the intensity of the Wassermann reaction, and caused the disappearance of the spirochaetes within twenty-four hours. Threatening secondary effects were never observed by the author, at the most slight stomatitis, mild headaches, and slight diarrhoea or colic occurred. If the injections cause local symptoms of irritation and pain, a little alypin or other local anæsthetic may be added to the solution. V. Lion achieved similar results. He injected asurol in doses of 1 to 3 c.c. of the 5 p.c. solution at intervals of two to four days. He usually administered it in series of 15 to 20 injections, which were on the whole well borne and only rarely gave rise to transient intestinal colic. This treatment proved especially satisfactory in the secondary symptoms of syphilis, whereas it appeared less effective in the later forms. The author believes that a combination of asurol and insoluble salts of mercury and salvarsan offers a prospect of success in suitable cases.

Atophan.

The mode of action of atophan** is discussed by G. Klemperer and J. Biberfeld, and their communications are all the more valuable since the mechanism of the action of atophan still awaits further elucidation. Weintraud attributed the action of atophan to the increased permeability of the kidneys produced by this drug and to the resulting increased excretion of uric acid, without any increase in the production of uric acid within the organism. Starkenstein,

* Merck's Reports 1909, 1910 and 1911.

Ijiri, *Japanische Zeitschrift für Dermatologie*, Vol. 11, No. 12.
Lion, *Archiv für Dermatologie und Syphiligraphie* 1912, Vol. 113, p. 713.

** Compare Merck's Reports 1911 and 1912.

Klemperer, *Therapie der Gegenwart* 1913, No. 6, p. 257.

Biberfeld, *Zeitschrift für experimentelle Pathologie und Therapie* 1913, Vol. 13, p. 301.

Weintraud, Merck's Report 1911, p. 162. *Therapie der Gegenwart* 1911, p. 97.

Starkenstein, *Archiv für experimentelle Pathologie* 1911, Vol. 63, No. 3 and 4. Compare also *Prager medizinische Wochenschrift* 1913, No. 3.

on the other hand, assumes that it effects an increase in the production of uric acid, caused by stimulation of the purin metabolism under the action of atophan, whereby nuclein material ready for resolution is more quickly destroyed and excreted. Biberfeld does not deny that it exerts an action on the kidneys, but does not consider it acceptable to assume that this effect is the only one to be taken into consideration, as in this case, in order to explain the action of atophan in healthy individuals, it would be necessary to assume that in these there is also a storage of uric acid, for the existence of which no proof has been adduced up to the present. Klemperer, too, expresses the belief that the mobilisation of uric acid is not the most important factor in the curative action of atophan, and inclines to the theory that this is due to a complicated antiphlogistic and analgesic action. However, it is not yet possible to offer an exhaustive explanation of the action of atophan. A. Schittenhelm and R. Ullmann also believe that the action of atophan is a very complicated one. But even were it possible to explain the relationship between the action of atophan and purin metabolism, this would still, according to H. L. Richartz, offer no explanation of the curative effect of atophan in rheumatism, as in this case it is improbable that the uric acid mechanism participates in the infection. Therefore, its mode of action in rheumatism is even less capable of explanation than in gout.

Friedeberg discusses the value of atophan in the treatment of gout, and expresses a very favourable opinion as to the value of the drug. Especially in early cases it proved very useful. He gave 1 gramme (15 grains) three times a day, and made the patient drink a bottle of mineral water during the day. He was unable to observe any difference in the action of atophan during a purin-free diet or on limiting the consumption of meat; however, the author believes that the observance of a purin-free diet during an attack of gout is justifiable for the reason that by this measure no increase in the already large endogenous content of uric acid can take place from exogenous sources. To

Schittenhelm-Ullmann, *Zeitschrift für experimentelle Pathologie und Therapie* 1913, Vol. 12, p. 360.

Richartz, *Deutsche medizinische Wochenschrift* 1913, No. 20, p. 953.

Friedeberg, *Fortschritte der Medizin* 1913, No. 12, p. 318.

deprive the patient of meat for a considerable period is, however, only justifiable if it does not weaken the patient too much. The action of atophan set in comparatively soon, the pains disappeared after the first or second dose, sleep was consequently undisturbed and the patient was able to move about in light shoes. The attack subsided by the third day, and the swelling rapidly disappeared under balneological treatment. Each patient received altogether from 8 to 10 grammes (120—150 grains) of atophan. In chronic gout the effect was not displayed so quickly as in acute cases; however, in no case did it fail entirely. Nevertheless, the effect of the drug on sleep was not so good as following the use of aspirin. Therefore, in suitable cases it is advisable as well as useful to supplement the atophan treatment by giving a nightly dose of aspirin of 0.5 to 1 gramme ($7\frac{1}{2}$ —15 grains). Dyspeptic symptoms were the only secondary effects observed, and occasionally the administration of the drug had to be suspended. It may be mentioned that atophan never failed when administered for the first time, but failures were observed when the treatment was repeated. In two patients, in spite of a prolonged interval and notwithstanding increased dosage, the author was unable to observe any action of atophan whatever after the third attack. In another case atophan failed to display its full effect already during the second attack.

In articular rheumatism atophan does not always succeed in bringing about the desired result, however, it deserves consideration in cases where salicylates provoke cardiac symptoms. Further, patients appreciate the absence of any diaphoretic action following the use of atophan, such as is the case with salicylates. On the other hand, atophan failed in monarthrits gonorrhoeica, and this was confirmed by R. H. Jokl. The latter, however, obtained satisfactory results with atophan in acute articular rheumatism, particularly in early cases. It effects a rapid abatement of the fever, pains and inflammatory symptoms, and puts an end to the migration of the articular affections. A daily dose of 2 to 4 grammes (30—60 grains) is given, and with this treatment Neukirch also effected a cure within twenty-four hours in the majority of cases, in which the use of salicylates had proved ineffective.

Jokl, Prager medizinische Wochenschrift 1913, No. 33.

Neukirch, Therapeutische Monatshefte 1912, No. 9.

The fact that atophan possesses antiphlogistic and antipyretic properties, as pointed out by some authors, induced G. Hahn to try it in septic diseases. In two cases of puerperal fever, in addition to collargol enemata (1 gramme [15 grains]), he gave for several days 1 gramme (15 grains) of atophan per os every two hours, up to a daily dose of 5 grammes (75 grains). In both cases the therapeutic effect of this treatment was remarkably good, however, it is difficult to say whether atophan or collargol was primarily responsible for this effect, or whether it was due to the combined action of both. Further trials must be undertaken to elucidate this point.

Secondary effects of an eczematous type following the use of atophan are reported by W. Hervick, A. von Müller, J. Philipps and E. de Oyarzabal. Müller prescribed atophan in a case of subacute articular rheumatism which had proved refractory to the usual treatment. He obtained a decided improvement, but after a short time he saw an elevation of temperature to 39.8° C., and a scarlatiniform eruption appeared. Oyarzabal observed the appearance of an eczema behind the ear after the use of atophan, which, after healing, again occurred when atophan was administered. In both cases these appearances may be ascribed to the atophan. Porges, too, observed the appearance of a generalized urticaria after the use of atophan, and Philipps saw skin eruptions in five cases treated by atophan.

Atoxyl.

F. Blumenthal reports a case of basal-celled ulcerated and sanious carcinoma of the upper eyelid, which had for months resisted X ray treatment. He therefore made use

Hahn, Prager medizinische Wochenschrift 1913, No. 26, p. 367.
Hervick, Journal of the American Medical Association, October 11, 1913.

Von Müller, Mitteilungen der Gesellschaft für innere Medizin und Kinderheilkunde, Wien 1913, No. 3, p. 45.

Philipps, Journal of the American Medical Association, September 27, 1913.

de Oyarzabal, Revista española de dermatologia y sifilografia 1913, No. 173.

Porges, Zentralblatt für die gesamte innere Medizin 1913, No. 2, p. 105, Vol. 6.

Blumenthal, Medizinische Klinik 1913, No. 20, p. 802.

of injections of atoxyl as an adjuvant to X ray treatment, and injected every week intravenously a dose of 0.2 gramme (3 grains) of atoxyl and 0.004 gramme ($\frac{1}{16}$ grain) of arsenious acid. The tumour, which was of the size of a small orange, soon began to break down and become clean and finally cicatrized. After five irradiations and twelve atoxyl injections the tumour had shrunk to one-fourth of its former size and extensive cicatrization had taken place. Blumenthal leaves it an open question whether a complete cure would have been obtained on continuing this treatment, nevertheless he considers the results achieved to be worthy of note.

As I already reported last year*, L. Arzt and W. Kerl were able to demonstrate that the toxicity of atoxyl is increased by liver emulsion, whereas this effect is not produced by lecithin. On continuing their pharmacological investigations the authors found that the addition of lecithin to atoxyl (and to a slight extent the addition of glycogen to atoxyl) was capable of increasing the parasitotropic action of atoxyl, as Levaditi had shown with his trypanotoxyl, obtained from liver emulsion and atoxyl. As regards parasitotropic action, however, the lecithin-atoxyl mixture is superior to trypanotoxyl. In contradistinction to atoxyl the parasitotropic effect of neosalvarsan is decreased by the presence of the above named substances.

Atoxylate of Mercury (Hydrargyri Atoxylas).

This preparation of arsenic and mercury**, introduced into materia medica by Uhlenhuth, was employed by G. Hügel in a large number of cases of syphilis. He used it in oily suspension, as recommended by Lesser***, and employed a freshly prepared suspension of 1 gramme (15 grains) of atoxylate of mercury in 9 grammes (150 min.) of oil of almonds for intragluteal injection. At first he administered doses of 0.05 gramme ($\frac{3}{4}$ grain), and if this dose was well borne he increased the amount at the next injection to 0.1 gramme ($1\frac{1}{2}$ grains). The injections were repeated twice a week until six injections had been given and a total amount of

* Merck's Report 1912, p. 111.

Arzt-Kerl, Wiener klinische Wochenschrift 1913, No. 1, p. 12.

** Compare Merck's Reports 1909—1911.

Hügel, Dermatologische Wochenschrift 1913, No. 10, p. 272.

*** Merck's Report 1909, p. 136.

0.55 gramme ($8\frac{1}{2}$ grains) had been reached. On the whole, the preparation was well borne, only the larger doses proved occasionally painful; abscesses or larger infiltrations, however, never occurred, and no other unwelcome symptoms worthy of note were observed. On the other hand, the curative effect was excellent. Immediately after the first injection the spirochætes disappeared, or they were injured and decreased, and usually disappeared after the second injection. The clinical symptoms were influenced in an equally striking manner. Scleroses, papules and condylomata generally showed a reaction after the first injection and usually healed after two to five injections. The curative effect of the preparation was especially marked on the lymphatic glands; its action on the Wassermann reaction was less evident, but this was possibly due to the short duration of the treatment.

The comparatively powerful curative action displayed by the small doses employed may be explained by assuming that the atoxyl acts as an amboceptor or mordant (Uhlenhuth), so that the mercury is able to attach itself very strongly to the cell. According to Hügel this explanation is in keeping with the observation he made that in spite of thorough care of the mouth stomatitis occurred more frequently among the cases treated with this preparation than is usual with other preparations of mercury, even on employing larger doses.

Only in one case out of thirty did the author meet with an unpleasant experience. In an otherwise healthy and strong man of 38 years of age the third injection was followed by severe cardiac failure. The author is of opinion that this was due to a cumulative action associated with idiosyncrasy to arsenic. The patient recovered completely on the following day and remained well. However, caution is advisable, especially as an idiosyncrasy to arsenic cannot be recognized beforehand, and care should be exercised if symptoms of intolerance occur after the first few injections.

Atropine Methylbromide.

Conclusions based upon practical experience induce P. O. Pribram to assume that the body offers two points of attack for sea-sickness — the labyrinth and the over-excited autonomous system. Unusual irritation of the labyrinth may

be avoided by placing the patient in a suitable position, i. e., in a recumbent posture, whereas irritation of the autonomous system is best prevented by the administration of atropine. Based upon these assumptions the author undertook experiments with atropine methylbromide. The prophylactic and curative use of this drug yielded good results, and it was very well borne*. As the internal administration of the remedy is not followed by an immediate result, owing to its slow absorption in the intestinal tract, the author also made use of subcutaneous injections of atropine sulphate. The latter proved much more effective when sea-sickness was already present. Thus, in one case he injected 0.001 gramme ($\frac{1}{64}$ grain) with complete success. Although the patient had vomited hourly and was in a pitiable psychical condition, these symptoms disappeared completely after the injection and he was able to go on deck and be present at all the meals, and remained free from any recurrences throughout the remainder of the voyage.

Pribram also draws attention to the statements of Byrne and von Noorden, which confirm the utility of atropine in sea-sickness, and encourage its further trial in this condition.

Atropine Sulphate.

The treatment of gastric affections by atropine appears to gain in interest of late. It was advocated by Riegel who founded its use scientifically on the sedative, antispasmodic and secretion-checking properties of atropine. In confirmation of this view D. Pletnew, Mathieu and Giraud also declare atropine to be a good remedy. In a large number of cases Pletnew found that atropine has a favourable effect on the secretion and allays the pain in disturbances of motility, hypersecretion, hour-glass stomach, pylorospasm, and gastric ulcer. Mathieu and Giraud obtained the same results in ulcers of the stomach, and based upon their experience they recommend the administration of atropine especially in acute

* The author gives no details regarding dosage. Compare Merck's Index 1910, p. 49.

Byrne, Physiology of the semicircular canals and their relation to seasickness. New York 1912.

v. Noorden, communicated by Pribram.

Pletnew, Russische medizinische Rundschau 1913, Vol. 79, p. 205.
Mathieu-Giraud, Presse médicale 1913, No. 36, p. 364.

cases with vomiting, pylorospasm and severe pains. It is best to begin with the use of morphine, to combat the pains already on the first day of treatment. This is followed by hypodermic injections of 0.00025 gramme ($\frac{1}{250}$ grain) of atropine sulphate, given three times a day, and from the third day 0.001 to 0.0015 gramme ($\frac{1}{64}$ — $\frac{1}{40}$ grain) of atropine sulphate is injected twice a day.

The successes obtained with atropine in the treatment of affections of the stomach induced F. Franke to try it in obesity. Particularly in patients who will not consent to a reduction in diet owing to a pronounced feeling of hunger and who can scarcely be compelled to observe this measure when under ambulatory treatment, atropine may yield good results. The author reports a case of obesity associated with fatty heart in which he prescribed a dose of 15 drops of tincture of belladonna, to be taken 15 to 20 minutes before each meal. This treatment led to an immediate decrease in the feeling of hunger, and the patient's weight decreased; the shortness of breath also improved. A relapse occurred after leaving off this treatment for some time, but on resuming it the same successful result was obtained as following its first employment. Franke recommends the further trial of his method, whereby the effect of belladonna on the gastric nerves, gastric secretion, gastric musculature and heart should be investigated.

J. Fischer was led to try the effect of atropine in sea-sickness starting from the assumption that this affection is due to stimulation of the vagus or of the autonomous system, in which case the selective action of atropine of inhibiting the vagus should exert a favourable effect in sea-sickness. His experiments justified this assumption. During a stormy passage he injected subcutaneously atropine sulphate (0.001 gramme [$\frac{1}{64}$ grain] for men, and 0.00075 gramme [$\frac{1}{90}$ grain] for women) into 52 passengers, most of whom were severely ill, and the effect of this measure was most striking. Within a few hours the patients felt much better, salivation and vomiting ceased, the sallow complexion improved, the pulse became fuller, in spite of a rough sea. After three to four hours the symptoms of sea-sickness had for the

Franke, Medizinische Klinik 1913, No. 25, p. 995.

Fischer, Münchener medizinische Wochenschrift 1913, No. 30, p. 1649.

most part entirely disappeared. Even in severe cases a cure could be effected by a single injection, and only in a few cases was it necessary to repeat the injection. Of special interest is the fact that no relapse occurred, even if the sea became rougher. On internal administration the effect of atropine was also plainly apparent, but was not so prompt or reliable as following its subcutaneous exhibition.

The value of atropine in sea-sickness has been confirmed by Byrne, von Noorden and Pribram.

According to Krasnogorsky the property of atropine of checking secretion proved useful in the treatment of bronchitic symptoms and in bronchopneumonia, and also as an adjuvant to the local treatment of eczema in infants. The author states that infants are able to tolerate comparatively large doses, without reacting by dilatation of the pupils or disturbances of the heart.

Atropine fails to act in diffuse parenchymatous inflammation of the cornea where the opacity has led to a decrease or suppression of the diffusibility of the cornea, although the considerable photophobia, lacrymation or even ciliary pains present in these cases would make a display of the action of atropine appear particularly desirable. In cases of this kind Wicherkiewicz advises a subconjunctival injection of one drop of a 0.25 p.c. solution of atropine sulphate, given once daily or every second day. If a neutral solution is employed containing cocaine the injection is almost painless. Should this form of application be excluded for any reason, before applying the atropine, a few drops of adrenalin or suprarenin solution may be instilled a few times until the surface of the cornea, as far as it is covered by vessels, has become blanched. The mydriatic action of atropine is often enhanced by this procedure, although it is not so reliable as following its subconjunctival injection.

R. Kaufmann and H. Donath report on the inverse action of atropine, but since their communications do not

Byrne and v. Noorden, communicated by Pribram.

Pribram, Wiener klinische Wochenschrift 1913, No. 22, p. 889.

Krasnogorsky, Monatsschrift für Kinderheilkunde 1913, p. 129.

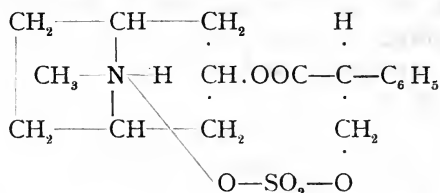
Wicherkiewicz, Wochenschrift für Therapie und Hygiene des Auges 1913, Vol. 16, No. 25, p. 201.

Kaufmann-Donath, Wiener klinische Wochenschrift 1913, No. 29, p. 1193.

lend themselves to brief abstraction, the original paper should be consulted.

Atropinesulphuric Acid.

Atropinesulphuric acid occurs in colourless crystals, melting at 238°—239° C. It is readily soluble in hot water, with difficulty soluble in cold water. It is insoluble in the usual organic solvents; it dissolves in dilute acids and in dilute solution of ammonia*. It has the following structural formula:



According to E. Kisch atropinesulphuric acid is intended for use as a substitute for atropine in ether anæsthesia, in which, as is well known, atropine is employed to prevent or diminish salivation. Atropinesulphuric acid also fulfils this purpose and is said to have the advantage of being considerably less toxic than atropine sulphate. The author, however, does not report any personal experiences bearing on this point. For his experiments he made use of a sterile solution of 0.02 gramme ($\frac{1}{3}$ grain) of pantopon (omnopon) and 0.001 gramme ($\frac{1}{64}$ grain) of atropinesulphuric acid, which was injected subcutaneously half an hour before inducing anæsthesia. Besides diminishing salivation the injection abolishes the stage of excitement.

The clinical study of atropinesulphuric acid by A. Philippstal has shown that it is an extremely efficient remedy for asthma, affection of the vagus, certain forms of tachycardia, night sweats of phthisis, and iodism. It does not appear to have any effect on morbid secretion of gastric juice. However, in such cases where it displays an action, the author is of opinion that its use is to be preferred to that of atropine sulphate since the secondary effects of the

* Compare Willstätter and Hug, *Zeitschrift für physiologische Chemie* 1912, Vol. 79, p. 146 and Trendelenburg, *Archiv für experimentelle Pathologie* 1913, Vol. 73, p. 118.

Kisch, *Münchener medizinische Wochenschrift* 1913, No. 7, p. 352. Philippstal, *Berliner klinische Wochenschrift* 1913, No. 46, p. 2145.

latter, such as dryness in the throat, acceleration of the pulse and excitation, are not observed with atropinesulphuric acid. In view of this advantage Philippsal regards the greater local painfulness caused by the subcutaneous injection of atropinesulphuric acid to be of minor importance. The single dose for internal and subcutaneous use is 0.001 gramme ($\frac{1}{64}$ grain) of atropinesulphuric acid.

Benzidine.

In an investigation of the Lafitte chloric acid reaction Pozzi-Escot found that benzidine might be advantageously used in the place of aniline for the detection of chlorates. He adopted the following modification of the Lafitte test: If 2 drops of a 10 per cent. solution of aniline sulphate are added to 1 c. c. of a chlorate solution and 4 c. c. of concentrated sulphuric acid are "layered" under this mixture, a blue ring appears even in the presence of $\frac{5}{100}$ mg. of chlorate. Nitrates and iodates, according to the author, cause the appearance of a reddish-brown ring. If benzidine is used in the place of aniline sulphate the test is made appreciably more delicate, and the presence of $\frac{5}{1000}$ mg. of chlorate can still be detected. Pozzi-Escot states that when using benzidine an orange-yellow ring is produced by chlorates as well as by nitrates and iodates.

C. Pertusi and E. Gastaldi employ benzidine for the detection of hydrocyanic acid. For this purpose a mixture of one drop of a 3 per cent. solution of copper acetate, five drops of a saturated solution of benzidine acetate and 0.5 c. c. of water is used. This reagent is coloured blue, or a blue precipitate is formed, by traces of hydrocyanic acid, and 0.000007 gramme of hydrocyanic acid is said to produce this reaction. In order to exclude the presence of other substances which may give the same reaction on oxidation, for instance, ferric salts, per salts, etc., the authors advocate a special procedure consisting in boiling the substance to be tested with solution of soda and then passing carbonic acid into the resulting solution in a suitable apparatus. The gas is then made to pass into the reagent, as it carries with it

Pozzi-Escot, Bulletin de la société chimique de France 1913, No. 10, p. 498.

Pertusi-Gastaldi, Chemiker-Zeitung 1913, No. 60, p. 609.

the hydrocyanic acid set free. Of course, this is the case only when the substance to be tested does not contain any metals which form double salts, such as iron and manganese, and therefore do not liberate any hydrocyanic acid under the action of carbonic acid. In this case the method must be suitably modified.

Benzin.

Several authors, including Pürckhauer, Levy and Hörrmann, have drawn attention to the fact that petroleum benzin, which is largely used per se or in combination with iodine for cleansing and disinfecting the skin before operations, has a caustic action, especially if its evaporation from certain parts of the body is retarded. A similar observation was made by E. Sehrwald on withdrawing blood (for the Widal reaction) from the lobe of the ear which he had previously rubbed with benzin. If the rubbing with benzin was performed while the patient was in a recumbent position a trace of benzin easily found its way into the auditory canal and might even reach the tympanic membrane. If this occurred the patients complained within a few seconds of extremely severe pain in the ear, which could only be removed by immediate copious irrigations. This led the author to close the ear with some cotton wool before disinfecting the lobe with benzin. This observation shows that the caustic action of benzin sets in almost immediately, and Sehrwald made use of it to investigate whether this effect might not be capable of therapeutic application. He states that benzin may be used in the place of mustard paper, croton oil, plaster of cantharides, etc., in cases where a slight or pronounced irritation of the skin is desired, provided its application is carefully supervised. In addition, by reason of its property of causing necrosis, benzin may be used to cause the decay and disappearance of superficial cutaneous growths. However, its application must be carefully localized, and its evaporation as much as possible prevented, which may be effected by covering the site with

Pürckhauer, Münchener medizinische Wochenschrift 1910, No. 42, p. 2186. Merck's Report 1910, p. 221.

Levy, Münchener medizinische Wochenschrift 1911, No. 6, p. 302.
Hörrmann, Münchener medizinische Wochenschrift 1911, No. 21, p. 1139. Merck's Report 1911, p. 276.

Sehrwald, Deutsche medizinische Wochenschrift 1913, No. 7, p. 318.

adhesive rubber plaster; the benzin should not be allowed to act for longer than is absolutely necessary. Careful experiments are required to establish to what extent neoplasms, deposits of pigments and infectious ulcers may be treated with advantage by benzin, and the fact must not be lost sight of that benzin is not absolutely harmless. The use of benzin for the disinfection of the skin as a preliminary to operations requires caution, and in this connexion it may be mentioned that C. Roux reports a few cases in which the copious use of benzin produced hæmaturia, in some instances associated with casts and leucocytes.

Benzol.

The benzol treatment of leukæmia* is exhaustively dealt with in the works of A. Pappenheim, A. von Koranyi, F. Tedesko, St. Klein, S. Stern, I. Sohn, A. Rösler, F. Billings, S. Wachtel, Kai Jespersen, W. Neumann, H. Reibmayr, W. Türk, J. Kardos, Aubertin and Parvu, H. Schur, Mohr, A. Sanguinetti, N. G.

Roux, *Korrespondenzblatt für Schweizer Ärzte* 1913, No. 16.

* Compare Merck's Report 1912.

Pappenheim, *Wiener klinische Wochenschrift* 1913, No. 2, p. 48.

Koranyi, *ibid.* 1913, No. 4, p. 147.

Tedesko, *ibid.* 1913, No. 4, p. 147.

Klein, *ibid.* 1913, No. 10, p. 357.

Stern, *ibid.* 1913, No. 10, p. 365.

Sohn, *ibid.* 1913, No. 15, p. 573.

Rösler, *ibid.* 1913, No. 21, p. 838.

Billings, *Journal of the American Medical Association*, February 15, 1913.

Wachtel, *Deutsche medizinische Wochenschrift* 1913, No. 7, p. 307.

Jespersen, *ibid.* 1913, No. 27, p. 1300.

Neumann, *Therapie der Gegenwart* 1913, No. 2, p. 56.

Reibmayr, *Medizinische Klinik* 1913, No. 14, p. 540.

Türk, *Wiener medizinische Wochenschrift* 1913, No. 10 and 11.

Kardos, *Budapesti Orvosi Ujsag* 1913, p. 45.

Aubertin-Parvu, *Société médicale des hôpitaux*, May 23, 1913. —

Revue de thérapeutique 1913, No. 12, p. 412.

Schur, *Gesellschaft der Ärzte in Wien*, May 2, 1913. — *Münchener medizinische Wochenschrift* 1913, No. 20, p. 1124. — *Revue de thérapeutique* 1913, No. 12, p. 412.

Mohr, *Münchener medizinische Wochenschrift* 1913, No. 38, p. 2146.

Sanguinetti, *Revue de thérapeutique* 1913, No. 16, p. 560. *Riforma Medica* 1913, No. 48, p. 1337.

Lutschewski, G. Királyfi, N. Liberow, E. Mühlmann, A. Gouget, A. Krokiewicz, Roedelius, Betke, Prusik, Klemperer and Hirschfeld.

These communications abundantly prove that benzol is a valuable remedy for the treatment of leukæmia. However, it should be used with discrimination, and it must be borne in mind that it is not absolutely harmless as is very apparent from the statements by Neumann, Pappenheim, Mühlmann, Liberow and Királyfi. Neumann reports a case of pronounced myelæmia and enormously enlarged spleen, in which the number of leucocytes was not particularly large (56 000 before adopting benzol treatment). Benzol was given for 36 days. There was a rapid reduction in the number of leucocytes (to about 5300), the enlargement of the spleen was reduced by about half, and the patient felt well. However, on discontinuing the drug it was found that it still displayed an after-effect. The number of leucocytes decreased to 200, the spleen continued to retract, fever, loss of strength, diarrhoea, epistaxis, fibrinous and then hæmorrhagic stomatitis and rhinitis were observed, and finally death occurred 39 days after the last dose of benzol. Based upon the result of the post-mortem examination, the author believes that after the benzol had exerted a beneficial influence on the leukæmia, in the end the patient's death was due to benzol poisoning. He therefore urges the utmost caution in using benzol. It is probably advisable to stop giving benzol as soon as a tendency to effect a reduction in the number of leucocytes is plainly manifest, and not to continue this treatment until the leucocyte count has reached a normal value. The fatal after-effect displayed by benzol in the case described above was confirmed by Királyfi, who reports a similar case which also ended fatally. An after-

Lutschewski, Russkij Wratsch 1913, No. 11. — Deutsche Medizinalzeitung 1913, No. 27, p. 461.

Királyfi, Wiener klinische Wochenschrift 1913, No. 26, p. 1062.

Liberow, Wratschebnaja Gazeta 1913, No. 16.

Mühlmann, Deutsche medizinische Wochenschrift 1913, No. 43, p. 2083.

Gouget, Presse médicale 1913, No. 14, p. 130.

Krokiewicz, Wiener klinische Wochenschrift 1913, No. 44, p. 1799.

Roedelius, Berliner klinische Wochenschrift 1913, No. 26, p. 1234.

Betke, Münchener medizinische Wochenschrift 1913, No. 45, p. 2545.

Prusik, Casopis lekaruv českých 1913, p. 940.

Klemperer-Hirschfeld, Therapie der Gegenwart 1913, No. 2, p. 64.

effect of benzol must be taken into account in every case, although incidents like those described do not justify the conclusion that benzol treatment is better avoided, as it has up to the present yielded excellent results in a large number of instances. Nevertheless, the question arises whether benzin, which is presumably less harmful than benzol, might not be used in the place of the latter. Pappenheim, who found that benzol exerted an injurious effect on the liver and the renal parenchyma, has already tried the use of benzin, and he states that in spite of the difference in their chemical composition both substances produce substantially the same results. He finds that benzin is better tolerated than benzol; at least comparatively large doses — 6 to 8 c. c. — were well borne by animals, and loss of appetite did not occur so quickly. On administering benzin mixed with double the amount of olive oil the same degree of changes in the bone marrow was produced as with benzol, with this difference, however, that the atrophy was not so marked. Irritation of the liver and kidney also occurred, but this was less frequent and assumed a milder form than following the administration of benzol. Pappenheim prefers the use of radio-active substances to that of benzol or benzin in the treatment of leukæmia, as the latter do not possess the same selective and radical action as displayed by irradiation. Koranyi, however, refuses to admit that Pappenheim's fears are justified, since his findings are based upon experiments on animals. Tedesko, too, believes that the daily dose of 3 grammes of benzol, suggested by Koranyi, may be safely given, and in his experience this amount has never given rise to any bad effects nor has he been able to observe any injurious action on the kidneys or on the general condition of the patients.

Klein administered benzol mixed with olive oil in capsules, and also in drops (up to 5 grammes a day), given in milk. The drug was well borne by the majority of his patients, some, however, did not tolerate it, and the author deprecates its use in the presence of bronchitic troubles and in tuberculosis. As regards dosage, Klein states that in mild cases and after X ray treatment much smaller amounts than those advocated by Koranyi and Királyfi may be given. Thus, in one case he gave 100 grammes (4 oz) of benzol in the course of 30 days, or on an average 3 grammes (60 min.)

per diem. Klein also tried subcutaneous injections of benzol, and for this purpose used a mixture of 2 grammes (40 min.) of benzol and 1.5 grammes (28 min.) of olive oil for one injection. As he observed symptoms of intoxication he soon reduced the dose.

In spite of these secondary effects, several of the authors mentioned above warmly advocate the use of benzol for the treatment of leukæmia, as they have found it extremely useful. If all the statements made are submitted to an impartial criticism, the conclusion may be drawn that the cautious use of benzol is justified; care should be taken, however, to avoid large doses and the treatment should be interrupted in order to apply X ray treatment during the interval.

The results of benzol treatment in leukæmia suggest that not only in leukæmia but also in carcinoma benzol may display an action similar to that produced by irradiation. Géza Királyfi was induced by this consideration to try the effect of intratumoral injections of benzol (0.1—0.5 c. c.) in mammary carcinoma. The result resembled that following the use of radiotherapy. The cells which came into immediate contact with the benzol were destroyed, the carcinomatous tissues underwent necrosis and were thrown off. However, the author states that this action is purely local, and the carcinoma cells in the neighbourhood of the broken down tissue continued to proliferate. Hence, it is not admissible to speak of a curative influence of benzol in carcinoma, and in this respect it is certainly not superior to X ray treatment, thorium, or operative intervention.

Benzoyl Peroxide.

As is well known, benzoyl peroxide is used technically as an oxidising agent. It is also used as a test in chemical analysis, and as a remedy in skin diseases and in burns, in the same manner as picric acid*. Recently St. Szécsi recommended it as a mordant in microscopic work. For his experiments he employed technical benzoyl peroxide, which is placed on the market under the name of "lucidol".

Királyfi, Berliner klinische Wochenschrift 1913, No. 43, p. 1984.

* Compare Merck's Reports 1905, p. 37; 1908, p. 146 and 1909, p. 142.

Szécsi, Deutsche medizinische Wochenschrift 1913, No. 33, p. 1584.

exhibition. The aqueous, acid solution of bismethylamino-tetramino-arsenobenzol hydrochloride is not suitable for this purpose.

Giemsa gives the following test for the recognition of this new preparation: 2 drops of dilute hydrochloric acid and 3 to 5 drops of a 0.5 p.c. solution of sodium nitrite are added to 5 c.c. of an aqueous solution (1:10,000) of the preparation, whereupon the mixture assumes a deep red colour. One part of the preparation in 100,000 parts of water can be detected by this test.

Pharmacological tests have shown that the preparation is comparatively slightly toxic. It was well borne and did not exhibit any marked neurotropic properties, nor any symptoms pointing to an injurious action on the eyes. Intravenous injection was the method best tolerated, but intramuscular and subcutaneous injections (of a not too concentrated solution) were also effective and did not give rise to any extensive infiltration or necrosis. The therapeutic effect of the preparation in fowl spirochaetosis, relapsing fever and scrotal syphilis was satisfactory and holds out a promise of its successful use in human medicine.

Induced by theoretical considerations and by his experience with similar arsenic compounds, Giemsa also tested hexamino-arsenobenzol, which differs from the above mentioned preparation in that the two methyl groups are absent. It proved even more effective in lues and relapsing fever, without exhibiting a greater degree of toxicity. The author intends publishing further details of his investigations.

Bismuth Subnitrate.

The fact that bismuth or nitrite poisoning* may, under certain circumstances, occur after the injection of bismuth subnitrate into fistulas has adversely influenced the value of the so-called "Beck's bismuth paste"**, the use of which has been described and recommended by several authors. Nevertheless, the use of bismuth paste deserves full consideration

* Compare Merck's Reports 1910—1912.

** Compare Pape, *Klinisch-therapeutische Wochenschrift* 1913, No. 13, p. 385. — Jensen, *Münchener medizinische Wochenschrift* 1913, No. 22, p. 1202. — Mayer and Boehr, *Zentralblatt für Chirurgie* 1913, No. 9, p. 320.

in suitable cases, for P. Reclus reports some cases in which it proved exceedingly useful and effected a cure where surgical treatment was not practicable or had proved ineffective, or would have led to extensive mutilation. In his opinion the use of the paste is especially indicated in the treatment of old-standing fistulas; however, before making the injection a careful examination should be made of the patient's constitution and condition of the intestines, and also of the extent of the fistula. The strength of the bismuth paste to be injected depends upon the amount required, thus if a small amount suffices a 20 per cent. paste is employed, otherwise a 5 per cent. paste is injected when a larger amount is required. The bismuth paste should be sterilized in a current of steam at 110° C. and kept in a sterile container. Before use the container is placed in water at 45° C., the contents are well stirred and the injection is made by means of a suitable syringe. The site of injection (orifice of the fistula) is disinfected with tincture of iodine, and the injection is made under slight pressure, so as to avoid causing any lesions or enlargement of the fistula. However, care must be taken to ensure the paste reaching all the folds, otherwise retention of secretion may occur with its associated unwelcome secondary effects. According to Reclus, three to ten injections are required in the course of five to fourteen days, as the paste must be washed out if there is profuse suppuration. Should any suspicious symptoms occur, further treatment is immediately suspended, and for this reason the patient must be kept under constant observation. Finally the fistula may be washed out with glycerin to remove all traces of bismuth subnitrate.

F. Rost makes the surprising assertion that the action of Beck's paste is by no means due to its content of bismuth subnitrate. In his opinion the healing effect displayed by the paste is due to the American vaseline it contains, and which possesses the property of stimulating proliferation of the connective tissue. Therefore, according to this author, the bismuth might be omitted, and a mixture of wax, soft paraffin and vaseline (5:5:60) employed for the same purpose. L. Wacker seeks the active principle of the bismuth paste in

Reclus, *Journal des praticiens* 1913, No. 30.

Rost, *Münchener medizinische Wochenschrift* 1913, No. 41, p. 2281.

Wacker, *Münchener medizinische Wochenschrift* 1913, No. 18, p. 2674.

the impurities contained in the vaseline and paraffin, which are present in greater amounts in crude liquid paraffin.

Bromoform-Ether-Amyl Nitrite.

Amyl nitrite, according to A. Heidenhain, is a drug which generally displays a reliable action on the state of contraction of the cerebral vessels in conditions of semi-consciousness of an epileptic nature. In two cases the author succeeded in causing the disappearance of the vascular contraction and at the same time of the condition of semi-consciousness by repeated inhalations of amyl nitrite. According to the author the use of this remedy is so simple and free from danger that it can be placed in the hands of every epileptic, with instructions to pour five or six drops into a cup and inhale the vapour on the first warning of an approaching epileptic attack. If the patient is not capable of recognising the signs which precede a fit, anyone in attendance can administer the drug. Of course, the administration of bromides and opium must not be omitted.

In a recent communication, Heidenhain states that he has tried a special mixture in the treatment of insomnia and migraine, and has found it effective. It consists of 3 grammes (18 min.) of bromoform, 5 grammes (95 min.) of amyl nitrite and 7 grammes (150 min.) of ether. He himself made use of this mixture with excellent results in intractable insomnia. It is used as follows: 12 to 15 drops of the mixture are poured into a cup and the vapour is inhaled through the nose and exhaled through the mouth, with the head averted from the cup. In the author's opinion this mixture should prove useful in epilepsy.

Bromural.

As bromural displays a selective action on the cerebrum without causing any injurious side effects, it is a useful sedative in dentistry and may be given to both adults and children. It is especially useful in the treatment of nervous and timid children, and both patient and dentist should benefit by its sedative action. A dose of 0.3 gramme (5 grains) of bromural usually suffices to remove the opposition of children within about twenty-five minutes; they evince a certain amount

of apathy and submit unresistingly to treatment, and fillings, injections and extractions may be made without encountering any difficulties of importance. Before undertaking more extensive operations, such as incision of the mucous membrane and chiselling, G. Ulkan gave to children over ten years of age 0.6 gramme (9 grains) of bromural and after twenty minutes was able to make the injection, and ten minutes later to conduct the operation to a successful termination. For instance, he was able by this means to resect three apices of root at one sitting in a nervous child without any opposition on the part of the latter.

H. Halasz, too, extols the sedative action of bromural, which he found extremely useful. He gave it especially when applying a bridge, grinding healthy teeth, in local anæsthesia and prior to every operation when the patient appeared to be particularly nervous. In his experience local anæsthesia is much more successful if bromural has been previously administered. Halasz, like Ulkan, found that bromural successfully overcomes the patients' dread of operation; they stated that they wanted to resist but did not possess the necessary energy to do so. According to the author's statements, one tablet is sufficient for children up to twelve years of age, and two tablets for adults.

S. Wassermann states that he has found bromural in combination with quinine of use in the treatment of whooping-cough. He reports a case of an eighteen months old child with a severe cough and bloody sputum, in which this treatment effected a considerable improvement in the cough and a condition of latency was established. Wassermann therefore suggests that treatment should be begun with veronal and quinine and then continued with bromural and quinine. In this connexion it may be mentioned that a dose of 0.07 to 0.15 gramme ($1\frac{1}{6}$ — $2\frac{1}{2}$ grains) of bromural can be given three times a day to children of about two years of age.

Y. Airila undertook a pharmacological comparison of the action of the two bromine compounds—adalin* and bromural.

Ulkan, Deutsche zahnärztliche Wochenschrift 1913, No. 15.

Halasz, Fogorvosi Szemle 1913, No. 1.

Wassermann, Therapeutische Monatshefte 1913, No. 10, p. 723.

Airila, Skandinavisches Archiv für Physiologie 1913, Vol. 28, p. 193.

* Bromural = monobromoisovalerianyl urea, Adalin = bromodiethylacetyl urea.

He found that the action displayed by both (in rabbits) was practically identical; adalin had a somewhat greater effect and the ratio of its lethal dose to that of bromural was 0.7:1 gramme per kilogramme of body-weight; it therefore follows that its lethal dose is lower than that of bromural.

Cacodylates*.

In veterinary practice, particularly in tuberculosis and distemper of dogs, the copper salts of dimethylarsinic acid (cacodylic acid) and of mono-methylarsinic acid are said to be useful remedies. According to L  pinay, copper cacodylate is a blue powder, soluble in water; copper mono-methylarsinate is an insoluble, blue powder. A dog weighing eight kilogrammes can tolerate a dose of 0.5 gramme of the former without injury, and of 0.3 gramme of the latter. However, to obtain a therapeutic effect it is not necessary to exceed a dose of 0.06 gramme (1 grain); therefore, the therapeutic dose lies far below the toxic dose.

The author used copper cacodylate in an aqueous solution of 1 in 300 for subcutaneous injection. He made the injection into the outer aspect of the hind-leg. The drug may also be applied intravenously.

L  pinay administered copper mono-methylarsinate internally in pills, in daily doses of 0.02 to 0.03 gramme ($\frac{1}{3}$ — $\frac{1}{2}$ grain). It causes neither vomiting nor diarrh  a; however, it reduces the temperature and causes a considerable increase in the number of leucocytes, by means of which an improvement in the general condition and a favourable influence on the course of the infection is effected.

Cactus Grandiflorus.**

Cactus (*Cereus*) grandiflorus, the liquid extract of which was for long held to be a good cardiac tonic, has suffered in reputation as a result of recent investigations. Apart from the fact that it was not possible to isolate the active principle of the drug, A. Hatcher and H. C. Bailey, who took great pains to

* Compare Merck's Report 1910, p. 1, or Merck's wissenschaftliche Abhandlungen No. 5.

L  pinay, Revue de pathologie compar  e 1912, November, Berliner tier  rztliche Wochenschrift 1913, No. 27, p. 487.

** Compare Merck's Report 1911.

Hatcher-Bailey, Journal of the American Medical Association 1911, Vol 51, p. 26.

secure samples of the genuine drug, found that it exhibited a slight cardiac action only when very large doses were administered. For this reason the results of a renewed investigation of the action of *Cactus* undertaken by A. Gröber are of interest. Following the procedure adopted in the preparation of alkaloids and glucosides, the author prepared from a large quantity of the drug a number of substances containing the active alkaloids or glucosides of the drug in as pure and concentrated a form as possible, and with only a slight amount of extractives and other impurities. According to the method of preparation adopted, these substances responded to the general tests for alkaloids, or to the glucoside reaction (with tannic acid). These results indicate that alkaloids and glucosides are present in *Cactus grandiflorus*, but, it is true, in very small amounts. Gröber's experiments show that these substances possess a cardiac action, resembling that of the substances of the digitalin group. In all his experiments on frogs he observed slowing of the pulse-rate, increase of systole; in two cases he observed slight cardiac peristalsis, and in one case stillstand of the ventricle in systole. The author ascribes this cardiac action to a glucoside which is also present with the alkaloids in *Cactus grandiflorus*. In view of the small amounts contained in the drug, Gröber is of opinion that *Cactus* is valueless as a cardiac tonic in human pathology, and cannot be used as a substitute for digitalis treatment.

Cadogel.

This new substitute for tar is prepared according to the directions of St. Bugarsky and L. Török by the fractional distillation of oil of cade; it is the fraction which distils over between 220°—300° C. at 20 mm. It occurs as a yellowish-brown, oily liquid with a slight odour of tar. It contains the curative and antipruritic substances of tar, but is almost entirely free from those substances present in tar which cause irritation of the skin. On exposure to the air it oxidises and assumes an intense brown colour. It is soluble in alcohol, ether, chloroform, acetone, benzol, etc., and is a powerful reducing agent.

Gröber, *Therapeutische Monatshefte* 1913, No. 8, p. 580.

Bugarsky-Török, *Wiener medizinische Wochenschrift* 1913, No. 26 and 27.

The preparation has proved useful in the treatment of eczemas. It was applied undiluted or diluted with alcohol (up to ten parts) with a brush to the skin, and the part covered with a gauze dressing. For infiltrated areas the part is covered with impermeable material; in mild cases talcum is applied after painting with cadogel. In some cases where the epidermis was intact the authors applied with a brush a concentrated solution in absolute alcohol. Usually one application daily is sufficient, and on no account should it be used more than twice, as otherwise it may cause irritation of the skin. Cases exhibiting peracute inflammation of the skin with large vesicular elevations of the epidermis should not be treated with cadogel. A further contraindication is severe suppuration complicating eczema. In this case an attempt should be made first to remove the complication by other means, e. g., moist compresses, and then make use of cadogel. Since the application of concentrated cadogel to the highly inflamed skin causes smarting lasting for one or two hours, the authors prefer the use of the diluted preparation, especially at the commencement of treatment; in mild cases where only a small area is affected it is applied in a concentration of $33\frac{1}{3}$ p. c., in cases marked by more severe inflammation and in which an extensive area is involved a dilution of 20 to 30 p. c. is employed. For this purpose the authors usually made use of vaseline, boric ointment (made with vaseline), zinc paste, etc., the cadogel being mixed with the diluent immediately before use. The amount of cadogel in the mixture was gradually increased until concentrated cadogel was applied, which then no longer caused smarting.

The results of the above cited authors were confirmed by A. Roth, J. Geber and I. Hidvégi.

Calcium Bromide.

Calcium bromide, CaBr_2 , occurs as a granular, white, very hygroscopic substance. It is readily soluble in water.

On the basis of theoretical considerations, calcium bromide should prove superior to sodium bromide in the treatment of laryngospasm and tetany, since the administration of calcium

Roth, Pester medizinisch-chirurgische Presse 1913, p. 197.

Geber, ibidem 1913, p. 199. — Zentralblatt der gesamten Arzneimittellkunde 1913, No. 18, p. 359.

Hidvégi, Wiener medizinische Wochenschrift 1913, No. 37.

displays an inhibitory effect on excited nerve tracts and thus assists the bromine action. For this reason L. F. Meyer recommends the use of calcium bromide. In order to test the efficacy of this salt and demonstrate its superiority over sodium bromide, B. Grünfelder tried it in a large number of children. In all cases of laryngospasm and tetany he prescribed a solution of 20 grammes ($\frac{2}{3}$ oz) of calcium bromide in 280 grammes ($9\frac{1}{3}$ oz) of water, of which 10 grammes ($\frac{1}{3}$ oz) were given to the children in food three times a day. Almost without exception no change was made in the food or diet. Among a large number of cases bromine acne was observed only once, nor did any intestinal disturbances occur which might be ascribed to the calcium bromide.

The author divided his patients into two groups. Those in the first group received sodium bromide, and after a relapse calcium bromide; those in the second group were given calcium bromide from the onset of the first attack. His results were as follows:

Sodium bromide displays a curative effect on the attacks in spasmophilic diathesis; however, its action is very slow. In six cases a period of freedom from attacks was established after from ten to sixteen days; in two cases it was found necessary to substitute calcium bromide for sodium bromide in order to effect this result. Further, in two cases treated by sodium bromide the observation was made that a relapse is not cured more quickly by the use of this drug; it follows, therefore, that the prompt action of calcium bromide is not solely due to the presence of a possible accumulation of bromine ions in the body. On the other hand, the author gained the impression that the attacks rapidly subsided in all cases of relapse in which calcium bromide was given instead of sodium bromide.

With regard to the patients in the second group, the author found that calcium bromide causes the disappearance of the acute symptoms in spasmophilic diathesis within a short time, i. e., within three to six days. Both during the first attack and in relapses its action is more rapid than that of sodium bromide. Therefore, Grünfelder considers calcium bromide the most efficacious mild narcotic for the treatment

of laryngospasm and tetany. The dose is 2 grammes (30 grains) a day.

Calcium Chloride and Calcium Lactate.

On the basis of Chiari's and Januschke's observations, who had found that the administration of calcium chloride exerted an inhibitory action on the exudative and transudative processes of the skin and mucous membranes, L. Weekers tried the use of this calcium salt in glaucoma, in the assumption that it might in this case also check the secretion of the intra-ocular fluid. In two cases he succeeded in obtaining a noteworthy success. One was a case of chronic inflammatory glaucoma, in which pilocarpine had failed to influence the high intra-ocular tension and acuity of vision; the other was one of simple glaucoma attended with progressive loss of vision. In both cases daily doses of 3 grammes (45 grains) of calcium chloride yielded excellent results. B. Tristaino was also able to confirm the action of this salt of reducing tension, both pharmacologically and clinically. In rabbits he observed after the subcutaneous injection of calcium chloride an appreciable diminution in the intra-ocular tension, also in the normal eye, which reached its maximum after about six hours. He used the drug in four cases associated with high tension and pain, in which it alleviated the symptoms. Like Weekers, he prescribed the following solution:

Calc. chlor. cryst.	9.0 grammes (135 grains)
Aq. dest,	120.0 „ (4 oz)
Syrup.	30.0 „ ($\frac{3}{4}$ oz)

M. Sig.: One tablespoonful three times daily.

With regard to the value of calcium treatment in spasmophilia* K. Blühdorn holds that lime is not a curative, but merely a good symptomatic. In his experience the visible spasmophilic symptoms abated after doses of 1 gramme (15 grains) of calcium chloride and the hyper-excitability of motor nerves to galvanic stimulation returns to normal. The latter is not appreciably influenced on continuing the lime treatment, whereas the spasmophilic symptoms disappear entirely. He made use of the following formula:

Chiari-Januschke, Merck's Report 1911, p. 183.

Weekers, Clinique ophtalmologique 1912, No. 6.

Tristaino, Archivio di ottalmologia 1913, Vol. 20, p. 589.

* Compare Merck's Report 1912.

Blühdorn, Berliner klinische Wochenschrift. 1913, No. 23, p. 1057.

Calc. chlorid. (sicc.) 10.0 grammes (150 grains)

Liq. ammon. anis. 2.0 grammes (40 min.)

Pulv. acac. 1.0 gramme (15 grains)

Saccharin. q. s.

Aq. dest. ad 200.0 grammes (7 oz)

M. Sig.: 10 c. c. ($\frac{1}{3}$ oz) to be taken six times a day.

In a few cases the author gave calcium chloride rectally, and to avoid irritation employed a solution containing not more than 2.5 p. c.

For medicinal use Blühdorn considers anhydrous calcium chloride in sticks to be the most suitable form as he found it the most satisfactory salt to prescribe. However, he admits that the better action of anhydrous calcium chloride is due to the fact that it contains more calcium than the crystalline salt. As the opinion expressed by the author might lead to an erroneous conclusion, the following facts should be borne in mind: Crystalline calcium chloride and anhydrous calcium chloride (providing pure preparations are used) differ only in that the former contains water, consequently they also differ in appearance, but when dissolved in water there is no difference in their pharmacological action. 1 gramme (15 grains) of crystalline calcium chloride is equivalent to 0.5 gramme ($7\frac{1}{2}$ grains) of anhydrous calcium chloride, as crystalline calcium chloride, $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$, contains 50 p. c. (exactly 50.68 p. c.), and anhydrous calcium chloride in sticks approximately 100 p. c. of CaCl_2 . The name of fused calcium chloride is given to a salt containing about 75 p. c. of CaCl_2 and 25 p. c. of water. Blühdorn employed anhydrous calcium chloride. With regard to dosage, as long as it is borne in mind that

Crystalline Calcium Chloride contains 50 p. c. CaCl_2

Fused Calcium Chloride „ 75 „ „

Anhydrous Calcium Chloride „ 100 „ „

it is immaterial which preparation is used. In their contributions to medical journals authors should be careful to distinctly specify the kind of calcium chloride used, and the same applies to prescriptions. In my opinion crystalline calcium chloride is best adapted for medicinal use as it is the most economical form to prescribe; the process of dehydration to which it must be submitted to obtain the other forms naturally entails an increase in the cost of production; thus, for instance, 0.5 gramme ($7\frac{1}{2}$ grains) of anhydrous calcium chloride costs about three times as much as 1 gramme (15 grains) of crystal-

line calcium chloride. In practice, too, the crystalline salt should prove more convenient to handle (in weighing, etc.). It may be mentioned that calcium chloride is not official in the German pharmacopœia, therefore, if a German author speaks of calcium chloride without specifying the form employed, this is usually taken to mean the crystalline salt. For subcutaneous injection crystalline calcium chloride is especially suitable as it yields a perfectly neutral solution.

Calcium treatment is discussed in a valuable paper by P. Saxl. In his experience a therapeutic effect is apparent only after administering calcium for several weeks. Thus, in hæmophiliacs a reduction in the time of coagulation of the blood was observed only after calcium lactate had been administered for two to four weeks. Further, in a severe case of hæmorrhagic diathesis the hæmorrhage disappeared only after three weeks. It therefore follows that although the oral administration of calcium is effective, it takes a considerable time to display its effect. He prescribed:

Calc. chlor.	20.0 grammes	($\frac{2}{3}$ oz)
Syrup.	40.0	„ (1 oz)
Aq. dest.	ad 400.0	„ (14 oz)

M. Sig.: 1 tablespoonful every 2 hours.

He also gave, particularly if constipation were present, 1 gramme (15 grains) of calcium lactate three times a day. The subcutaneous or intramuscular injection of calcium salts should prove more effective; however, either form of exhibition causes intense irritation. This led the author to try a combination of calcium chloride and sterile gelatin solution*. The injection of this calcium chloride gelatin, to which the name of "kalzine" has been given, presents the advantage that the gelatin assists the calcium action. Saxl used kalzine in the treatment of a large number of hæmorrhagic diatheses of all kinds, such as purpura hæmorrhagica, hæmophilia and scurvy, and obtained a successful result in almost every case. Profuse hæmorrhages were arrested by one to three injections and did not recur for a considerable time. Persistent gastric hæmorrhage in ulcer of the stomach and hæmoptysis of tuberculotics were

Saxl, Medizinische Klinik 1913, No. 15, p. 578. — Compare also R. von den Velden, Therapeutische Monatshefte 1913, No. 10, p. 685.

— M. Kochmann, Deutsche medizinische Wochenschrift 1913, No. 45, p. 2190.

* Compare Merck's Report 1912, p. 427.

favourably influenced by the injections, while nephritic renal hæmorrhages did not react. Compared with the subcutaneous or intramuscular exhibition of kalzine, the oral administration of calcium lactate (1 gramme [15 grains] 3 times a day) in hæmophilia, purpura, etc., had to be continued for several weeks before an appreciable shortening of the time of coagulation of the blood became apparent.

The internal administration of calcium lactate for several weeks in two cases of œdema fugax succeeded in preventing the recurrence of any swellings for a period of six months during which the patients were kept under observation.

Injections of calcium also proved very useful in bronchial asthma not complicated by chronic bronchitis. The author therefore recommends an injection of calcium-gelatin during the attack, to be repeated if necessary, and followed by prolonged treatment with the preparation administered per os. Trials with the preparation in tetany are also advised, although a successful result appears doubtful in these cases. On the other hand, calcium treatment may prove distinctly useful in Graves's disease, and further indications for its use might be found in the treatment of various conditions of irritation, such as diabetes insipidus, hyperemesis, and paralysis agitans. In this connexion a paper by R. Emmerich and O. Loew on the influence of lime salts on the constitution and health is of interest. The authors found that healthy as well as sick persons benefit by taking calcium chloride, and give the following directions for its use:

Calc. chlor. cryst. 100.0 grammes ($3\frac{1}{3}$ oz)

Aq. dest. 500.0 „ (17 oz)

M. Sig.: 1 teaspoonful 3 times a day, at meals, to be taken in food, or diluted with water.

Or, according to the authors, calcium bread (bread containing calcium chloride) may be used in the place of the above solution. In illnesses in which a loss of lime is apparent in the urine, the use of calcium lactate is more suitable, to which may be added sodium tartrate in order to increase the alkalinity of the blood. For this purpose a mixture of equal parts of calcium lactate and sodium tartrate is prepared of which 2.5 to 3 grammes (40—45 grains) are taken three times a day, during meals.

During the past year I have been frequently asked whether the prolonged use of calcium salts is quite free from any

injurious effect. However, I do not feel competent to answer this question. M. Jacoby and G. Eisner report that several functions of the kidneys are adversely influenced by calcium salts; they state that the excretion of chlorides is reduced and consequently swellings are produced. They also found that the decrease in the excretion of sugar in diabetes is due to the calcium causing impermeability of the kidneys. On the other hand, Emmerich and Loew maintain that calcium treatment, if carried out in accordance with their instructions, is quite harmless (see below).

Mention may also be made of a paper by Rothberger and Winterberg, in which the influence of injections of calcium chloride on the action of the heart is discussed.

According to H. Pribram calcium lactate may prove very useful in epilepsy. The author administered to a boy a spoonful of a solution containing 3 grammes (45 grains) of calcium lactate and a spoonful of a solution containing 3 grammes (45 grains) of sodium bromide alternately, with the result that the fits, which had occurred every half hour, disappeared permanently. The bromine treatment previously adopted had failed to produce a similar success.

H. Januschke reports on the internal administration of calcium salts in the treatment of "colds". He states that daily doses of 10 to 14 grammes of calcium lactate ($\frac{1}{3}$ — $\frac{1}{2}$ oz), given to children and adults, yield excellent results in acute and chronic rhinitis; a commencing "cold" may be arrested by this treatment, and the occurrence of iodine coryza can be effectively prevented. It is also said to have proved useful in hay fever. This action is most probably due to the property of calcium of checking exudation, and Januschke believes that the calcium reduces the permeability of the walls of the vessels and of the connective tissue of the mucous membrane for liquid exudates.

Emmerich and O. Loew attribute the unsatisfactory results of calcium treatment in hay fever to the fact that usually

Jacoby-Eisner, *Deutsche medizinische Wochenschrift* 1913, No. 34, p. 1657.

Rothberger-Winterberg, *Pflügers Archiv für die gesamte Physiologie*, Vol. 142, No. 7 and 8.

Pribram, *Prager medizinische Wochenschrift* 1913, No. 33, p. 466.

Januschke, *Zeitschrift für Balneologie* 1913, No. 9.

Emmerich-Loew, *Münchener medizinische Wochenschrift* 1913, No. 48, p. 2676.

lime salts are administered only shortly before the attack and for not longer than eight days. Basing on their experience the authors state that it is necessary to administer for a long time, for several months or even years, daily amounts of 3 grammes (45 grains) (of crystalline calcium chloride), and they prescribe the following solution:

Calc. chlor. cryst. 100 grammes ($3\frac{1}{3}$ oz)

Aq. dest. 500 „ (17 oz)

M. Sig.: 1 teaspoonful to be taken in the morning, at midday and in the evening, with meals, in water, soup or coffee.

This treatment succeeds within a few weeks in causing the disappearance of the more important symptoms of this idiopathic disease, and in the course of years of all the symptoms of hay fever.

In disturbances of nutrition in infants von Aschenheim recommends the addition of calcium lactate to the food. This medication proved useful in slight alimentary dyspepsias, infectious dyspepsias and digestive disturbances in rickets.

Calcium Tungstate in Crystals.

Calcium orthotungstate, CaWO_4 , occurs in the form of white crystals; calcium paratungstate, $\text{Ca}_3\text{W}_7\text{O}_{24} \cdot 18\text{H}_2\text{O}$, is a white crystalline powder. Both salts are insoluble in water.

The ortho salt becomes phosphorescent under the influence of X rays. Therefore, as is well known, calcium orthotungstate is employed as an intensifier in making radiographs, as it emits chemically very active ultra-violet rays, in addition to the visible bluish-white rays of light. H. Krukenberg tried the use of this salt as a new source of light, capable of application to any part within the human as well as animal organism where a display of its properties is desired. The author hoped by its aid to appreciably increase the strength of weak X rays, radium or mesothorium radiations, and in this he was successful.

When X rays impinge on calcium tungstate, injected subcutaneously into animals, it becomes phosphorescent, and under

Aschenheim, Monatsschrift für Kinderheilkunde 1913. — Zentralblatt für die gesamte Therapie 1913, No. 11, p. 603.

Krukenberg, Münchener medizinische Wochenschrift 1913, No. 38, p. 2112.

certain circumstances it still exhibits this property with undiminished intensity even after a period of forty days, and causes blackening of a photographic plate at a distance of 4 cm.

In order to test the action of calcium tungstate, or of the rays it emits after being submitted to the influence of X rays, the author made an intratumoral injection of 0.4 gramme (6 grains) of calcium tungstate (suspended in normal saline solution) into a patient with cancer of the breast; X ray treatment was applied on the following three days and then amputation of the breast was performed. It was then found that in the neighbourhood of the site of injection necrosis and degeneration of the cells of the tumour had set in, but this had not taken place in any other part. The action decreased with increasing distance from the site of injection.

Calcium tungstate apparently possesses an action in tuberculosis when submitted to X ray irradiation, as Krukenberg was able to establish by experiments on animals. Hence calcium tungstate may prove a valuable adjuvant to the radiotherapeutic treatment of malignant tumours and tuberculosis.

Calotropis Procera. (Calotropin.)

A plant exhibiting an action on the heart similar to that of digitalis is described by L. Lewin. This is *Calotropis procera* R. Br. (*Asclepias procera* L.), which has been known to botanists for a considerable time and which is fairly common in Africa and in Southern Asia, and has been used therapeutically from ancient times*. Parts of the plant are still in use to-day, especially in India, as remedies for asthma and headache, and, according to Lewin, also for skin diseases, syphilis, leprosy and dysentery. The latex of *Calotropis* is said to have been used as an arrow poison.

Lewin has investigated and described the latex of *Calotropis*. Special interest attaches to the action and the active principles of this drug. Its use as an arrow poison, and for poisoning and committing suicide, as has been observed with Indians, points to the fact that it contains one or more substances

Lewin, Archiv für experimentelle Pathologie 1913, Vol. 71, p. 142.
— Medizinische Klinik 1913, No. 6, p. 206.

* Compare Warden and Waddel, American Journal of Pharmacy 1885, Nr. 5, p. 165. — Archiv der Pharmazie 1885, Vol. 23, p. 547. — Dragendorff, Die Heilpflanzen 1898, p. 547.

with a toxic action. These are, according to Lewin, contained in the serum of the latex, which can be obtained as a clear, or slightly turbid liquid after removing the white resin (alban = $C_{16}H_{27}O$). If the inactive albumin is removed from this liquid and the resulting bitter tasting fluid is concentrated in a vacuum, it evolves an odour resembling that of coniine. The author did not succeed in isolating this odorous principle. On further concentrating the liquid a light brownish, later blackish mass is separated, which is soft while warm and solidifies on cooling. It is only slightly soluble in cold water, more soluble in boiling water, from which it is again precipitated on cooling. It dissolves with a greenish fluorescence in alcohol containing water. Dried over sulphuric acid it yields a yellowish-brown powder which softens on exposure to the air, and which, according to Lewin, contains the principle of *Calotropis* possessing an action on the heart. After purification with alcohol and ether it occurs as an amorphous, very hygroscopic substance, readily soluble in water with neutral reaction. It contains no nitrogen and burns with a luminous flame. It is coloured blood-red by concentrated sulphuric acid. If traces of the white resin are still present in the substance the red colour changes after a short time to green.

The preparation obtained and purified by the above described method is stated by Lewin to be the active principle of *Calotropis procera*, and is called by him calotropin.

If 0.001 to 0.003 gramme of calotropin in aqueous solution is injected subcutaneously into frogs, peristalsis of the heart occurs after about three minutes, and after about six minutes the heart stops in systole. In rabbits the injection of 0.02 to 0.04 gramme into the subcutaneous tissue after two minutes causes the animals to lick, then râles become audible, followed by putting the head forward and dyspnoea, then tremor of the head, gradual drooping of the head, tremor of the muscles of the trunk, and the animal dies in convulsions after twenty to thirty minutes under increased respiratory embarrassment.

Calotropin serum, which will keep for years, according to Lewin, can be used clinically as a heart tonic, and for this purpose is administered per os or subcutaneously. Further details regarding its use and dosage are not at present available.

Camphor.

To introduce camphor into the blood-stream, for instance in the treatment of pneumonia, hitherto an oily solution has usually been employed which is injected subcutaneously. Since it may be assumed that from these deposits of camphor the camphor passes but slowly into the aqueous blood fluid and therefore only small doses are able to display their action within a given time, even when large amounts of camphorated oil are injected into different parts of the body, there is reason to assume that the intravenous injection of an aqueous solution of camphor, in spite of the fact that camphor is only slightly soluble in water, would permit the introduction of far larger amounts of camphor into the blood-stream. Nevertheless, the amount of camphor which is soluble in water and which was definitely established by H. Leo, should prove quite sufficient to display an effective therapeutic effect. This author states that camphor is soluble 1 in 500 of water, whereas hitherto, based upon the statements in the literature, its solubility was assumed to be only 1 in 1,000. During these investigations the interesting fact was established that camphor is less soluble in hot water than in cold water. Therefore, a saturated solution of camphor cannot be obtained by boiling, and the solubility of camphor has been undervalued.

According to Leo, the intravenous injection of a saturated aqueous solution of camphor (0.2 p. c. in Ringer's solution) displays all the known effects of camphor in a typical manner. This action is considerably more intense than following the subcutaneous injection of camphorated oil, not only in that it sets in much quicker but also inasmuch as the effect displayed is far more powerful than when an even much larger dose of camphor in oily solution is injected. The duration of the action displayed by the aqueous solution is also by no means shorter than that of camphorated oil. Hence the results so far obtained in the trials with an aqueous solution of camphor speak in favour of its specific action in pneumonia.

Leo, Deutsche medizinische Wochenschrift 1913, No. 13, p. 591 and No. 15, p. 690 and Münchener medizinische Wochenschrift 1913, No. 43, p. 2397. At the author's suggestion I supply sterile, 0.142 p. c. camphor water in sealed ampoules (containing 25 and 40 c. c.), and in glass-stoppered bottles (of 100 and 200 c. c.)

In continuation of Leo's statements W. Weintraud reports the results of his experiments with camphor water, undertaken by him some years before. He employed a 0.1 p. c. solution of camphor in water which he injected into the vena media in amounts of 250 to 350 c. c. The injections were borne without any reaction and never caused any local symptoms of irritation. However, Weintraud says that the results in practice did not surpass those usually observed after the subcutaneous or intramuscular injection of camphorated oil. The author, who lays special stress upon the action of camphor on the heart, fears that the intravenous injection of comparatively small amounts of camphor dissolved in water will not succeed in replacing the injection of camphorated oil, which in his experience displays a prompt and full effect. However, in cases where the injection of larger amounts of fluid into the vascular system is indicated, for instance after great loss of blood, it is advisable to use the camphor water proposed by Leo in the place of ordinary normal saline solution, as experience has shown that it causes neither local vascular changes nor nerve disturbances.

In a number of cases of pneumonia Weintraud, like Seibert, injected intramuscularly 12 c. c. of 20 p. c. camphorated oil twice daily. He found that the 4.8 grammes of camphor incorporated daily by this measure were well borne by most patients; however, the results were not entirely satisfactory. In several cases, it is true, an influence on the temperature curve of patients suffering from pneumonia was apparent in that the morning remissions occurred earlier and more frequently than is otherwise the case; however, the fever did not disappear until the fifth or seventh day. As already stated, the author lays great weight upon the action of camphor on the heart*.

E. Roser expresses the same opinion and considers the use of camphor in pneumonia to be indicated on the occurrence of a fall in blood pressure, in order to effect a rise in pressure. In acute croupous pneumonia he advocates the use of large

Weintraud, Deutsche medizinische Wochenschrift 1913, No. 28, p. 1352.

* Compare J. Isaak, Pflügers Archiv für die gesamte Physiologie Vol. 153, No. 9 and 10.

Roser, Wiener klinische Rundschau 1913, No. 23, p. 353 and No. 24, p. 373.

doses in the form of subcutaneous injections of camphorated oil. They increase the strength of the affected heart and with it the blood pressure and pulse; an antibacterial action is produced and the temperature is lowered. The author never observed the occurrence of unwelcome sequelæ, such as conditions of excitement or toxic symptoms.

Certain also obtained very good results with large doses of camphor in pneumonic and broncho-pneumonic affections. He employed a 20 p. c. solution of camphor in olive oil purified by alcohol, which he usually injected intramuscularly. For adults he gave in cases of moderate severity daily doses of 10 c. c., and in severe cases 20 c. c. (in two doses). Children were given 1 c. c. for every year of their age. For children this is a very large dose and this fact must not be lost sight of, especially as M. Perrin warns against the use of concentrated camphor ointments in children, even on endonasal application. He reports the case of a nine weeks' old infant which became collapsed after the application of camphor ointment.

E. Schmidt also advocates the use of large doses of camphor. His method consists in injecting, with strict aseptic precautions, 5 to 10 c. c. of 20 p. c. camphorated oil once or repeatedly, according to the case, until a definite effect is apparent. He states that in 55 cases of pneumonia, including 5 adults and 50 children ranging in age from 7 months to 16 years, all the patients were cured by this treatment. In 31 cases a critical fall in temperature, and in 24 cases a lytic fall in temperature with a shortening of the duration of the illness was observed. In over 50 p. c. of the critical cases the fall in temperature occurred after a single injection already within two to twenty-four hours. The doses mentioned above were well borne and did not cause any clinical toxic symptoms.

H. Roziès and M. Arrivat also advocate the use of large doses of camphor for subcutaneous and intramuscular injections. The indications for this treatment are: sepsis, acute peritonitis, bronchitis, pneumonia, shock consequent on opera-

Certain, *Presse médicale* 1913, No. 20, p. 196.

Perrin, *Annales de médecine et chirurgie infantile* Vol. 16, p. 443.

Schmidt, *Petersburger medizinische Wochenschrift* 1913, No. 15, p. 180.

Roziès-Arrivat, *Journal des praticiens* 1913, No. 15.

tions, infectious diseases, myocarditis, gastro-enteritis in children, etc. For injection they recommend a solution of 10 grammes of camphor in 10 grammes of ether and 80 grammes of olive oil. The authors state that daily doses of 30 to 40 grammes, and even as much as 100 grammes, are well borne by adults.

With regard to the action of camphor on the heart reference may be made to a work by J. D. Heard who studied both clinically and experimentally the action, toxicity and curative value of camphor. It may be stated that the author does not consider camphor to be a cardiac stimulant.

On the other hand, L. Fornaca and R. Lanza maintain that camphor is a useful cardiac tonic, as it increases the blood pressure and the viscosity of the blood; however, they state that the large doses advocated by other authors are unnecessary since the customary doses are quite sufficient. Camphor is powerless in the presence of infections, and neither in large nor in small doses is it capable of displaying a bactericidal action on virulent pathogenic bacteria. Nevertheless, camphor appears to afford a certain amount of protection, as is apparent from the pharmacological investigations of K. E. Boehncke, at least in pneumococcal infections.

As is apparent from the foregoing statements, opinion is still divided regarding the pharmacological action, the therapeutic value and the dosage of camphor. The same applies to the use of camphor in peritonitis. Blecher, Hugel and Döderlein report upon its use in this indication*.

Blecher injected intraperitoneally 1 p. c. camphorated oil in five cases of appendicectomy, and usually obtained an immediate success. The well-being of the patients on the following day, compared with the severe aspect of the disease on the preceding day, the fall in temperature and the good pulse are attributed by the author to this treatment. In all cases,

Heard, American Journal of the Medical Sciences 1913, February.

Fornaca-Lanza, Riforma medica 1912, No. 50.

Boehncke, Berliner klinische Wochenschrift 1913, No. 18, p. 818.

Blecher, Münchener medizinische Wochenschrift 1913, No. 23, p. 1261.

Hugel, Beiträge zur klinischen Chirurgie 1913, Vol. 83, p. 606.

Döderlein, Zentralblatt für Gynäkologie 1913, No. 9, p. 312.

* Compare also: Offinger, Bakterizidie des Kampfers. Dissertation Stuttgart 1912. — Zentralblatt für Bakteriologie 1913, Vol. 59, No. 15, p. 454 (Ref.).

however, one complication resulted from the use of camphorated oil, i. e., a Douglas' abscess. The author believes that this complication can be avoided by suitable drainage. Döderlein also reports two cases of abdominal operations in which the successful result spoke in favour of the use of camphorated oil. On the other hand, Hugel's experience of this method was unsatisfactory. In two cases of appendectomy he observed a retardation of the healing process and metastatic suppuration, and in a case of perforation of the gall-bladder sopor, tetanus and finally death under symptoms of poisoning. For this reason the author warns against the use of camphorated oil in biliary peritonitis.

Camphor has also proved useful in the treatment of tuberculous fever. With subcutaneous injections of 20 p.c. camphorated oil K. Weihrauch succeeded in causing the disappearance of the fever, or a marked fall in temperature, in about 20 p.c. of the cases, while the morbid processes also showed an improvement. The author is unable to explain the action of camphor, but assumes that it displays an inhibitory influence on the excitors of the mixed infection, in addition to possessing anticatarrhal properties. The harmlessness of camphor injections justifies a more widespread trial of camphor treatment, all the more as Weihrauch found it useful when all other methods had failed to cause defervescence.

Carbolic Acid.

For the rapid and complete extermination of head-lice A. Whitfield employs a 2.5 p. c. solution of carbolic acid, which is devoid of danger when used in this strength. The author's method is especially useful in girls over five years of age who already have long hair, which is not to be sacrificed. The patient is laid on her back with the head over the edge of the couch, and beneath the head is placed a basin containing the solution of carbolic acid. The hair is thoroughly soaked with the solution, and special care is taken to secure thorough saturation of the hair over the ears and at the nape of the neck, since these parts are the sites of predilection of the parasites. This sluicing is carried out for ten minutes; the hair is allowed to drain and the whole head is swathed in house flannel,

fastened so as to form a turban, and the head is allowed to remain like this for one hour. With the treatment the pediculi as well as the nits are completely destroyed; any impetiginous scabs are softened so that they come away easily when an ointment is applied.

A. N. GuljaJeff expresses himself highly satisfied with the effect of Baccelli's method of treating tetanus by phenol. He treated two cases with complete success by this method. In the one case tetanus developed eight days after an injury to the foot. Treatment with curare proving ineffective, the author injected every four hours 2 c. c. of a 3 p. c. solution of phenol. On the third day of treatment a striking improvement was apparent. The action of phenol received a striking confirmation when the injections were stopped too soon, whereupon convulsions immediately recurred. The author injected altogether 14.5 grammes of carbolic acid, up to 0.48 gramme daily. The second case was one of head-tetanus with several wounds of the head, which was cured in a fortnight after using 5.4 grammes of phenol.

Cerium Nitrate, Highest Purity.

Pure cerium nitrate, $\text{Ce}_2(\text{NO}_3)_6 + 12\text{H}_2\text{O}$, occurs in the form of white transparent crystals, which are readily soluble in water.

The investigations of J. Bekk have shown that cerium dioxide is a suitable contact substance for the analytical destruction of organic matter. For this purpose cerium dioxide asbestos is prepared by treating asbestos with a saturated aqueous solution of cerium nitrate, the asbestos is then dried and heated to redness. The cerium dioxide asbestos obtained by this means has a light yellow colour. If inflammable gases, such as the vapours of benzol, naphthalene, anthracene, anthraquinone and phenanthrene quinone, are made to pass in a current of oxygen over this prepared asbestos, heated to redness, complete combustion to water and carbon dioxide takes place. In the case of organic compounds containing nitrogen the oxides of nitrogen which are formed in the combustion tube are absorbed by passing into a receiver containing lead

GuljaJeff, *Russkij Wratsch* 1912, No. 28.

Bekk, *Berichte der deutschen chemischen Gesellschaft* Berlin 1913, Vol. 46, p. 2574.

peroxide heated to about 300° C. according to Dennstedt. The only alteration which the contact substance undergoes on continued use consists in the long-fibred asbestos disintegrating to a light powder, but otherwise its usefulness is not impaired. In the combustion of substances containing sulphur, however, the cerium dioxide takes up SO_2 which it gives off only when strongly heated. If it is then heated in the oxygen blow-pipe flame to a bright red heat it yields no more SO_2 and can be used again, as its contact action is not impaired.

Charcoal, Animal

As was stated in my Annual Report for the year 1911, the internal administration of animal charcoal has of late been advocated as a therapeutic measure in poisoning by mushrooms or by minerals, and also in enteritis. H. Pribram found it useful in particular in persons suffering from atony of the stomach and intestines associated with meteorism. In order to facilitate the administration of animal charcoal and to increase its absorbent effect, I now supply a specially prepared product under the name of "Animal charcoal, highest purity, in fine powder, for internal use".

As is well known, powdered charcoal has also been used in the treatment of wounds. A peculiar kind of powdered charcoal was employed by F. Hammer, who roasted sawdust of hard wood (oak and beech) in a crucible and made use of this *scobis tosta* as a wound dressing. According to his report, this preparation possesses an enormous absorptive power, is very plastic and can be introduced in large amounts into wound cavities. Mixed with 10 p.c. of iodoform it proved especially useful in soft chancres, moist gangrene, suppurating gummatous wounds of bones and incised buboes. For the dry treatment of the vagina it cannot be employed per se, as it adheres too firmly to the mucous membrane. For this purpose a mixture of equal parts of the preparation and kaolin is employed; or the preparation is applied enclosed in small bags of gauze, but in this form it does not act so well. As soon as the wounds become clean it irritates and its use must be abandoned.

Pribram, Prager medizinische Wochenschrift 1913, No. 33, p. 466.
Hammer, Münchener medizinische Wochenschrift 1913, No. 21, p. 1150.

K. O. Larsson describes a method for the estimation of chlorine in the urine and in blood, in which he makes use of Merck's pure blood charcoal for analysis. This preparation has the property of adsorbing from the above mentioned body fluids all substances which react with silver nitrate, with the exception of chlorides, which remain in solution. For this purpose 20 c. c. of urine and 1 gramme of charcoal are allowed to stand for ten minutes, shaking frequently, the mixture is then filtered and the amount of chloride present in 10 c. c. of the filtrate is determined by titration with silver nitrate according to Mohr. In the analysis of blood, coagulation of the latter (5—10 c. c.) is effected by means of 50 c. c. of a 2 p. c. solution of magnesium sulphate and acetic acid, on a boiling water-bath; after cooling, the mixture is made up to 100 c. c. with water and 3 grammes of charcoal are added, with shaking. 50 c. c. of the filtrate are used for titration.

In urines in which besides glucose other reducing-bodies are present, the latter may be removed by treatment with "blood charcoal purified with acid", whereupon the glucose test becomes more specific. Sydney W. Cole found that this preparation of charcoal (and none other) adsorbs all reducing substances, but leaves the glucose in solution. He therefore suggests the following method for the estimation of glucose: 10 c. c. of urine and 1 gramme of blood charcoal are heated to boiling, with constant shaking, cooled and filtered. 0.5 gramme of sodium carbonate and 6 drops of glycerin are added to the filtrate, which is then heated to boiling, and 4 drops of a 5 p. c. solution of copper sulphate are added. The presence of glucose is apparent by the precipitation of red cuprous oxide.

Chenopodium Oil.

The oil of *Chenopodium anthelminticum*, which has already been repeatedly mentioned in my Reports*, appears to be gaining in interest, particularly in the treatment of ascariasis. A case of this kind is reported by J. Przedborski. A boy, aged two years and three months, who was suffering from tuberculous meningitis also harboured a large number of worms

Larsson, *Biochemische Zeitschrift* 1913, Vol. 49, p. 479.

Cole, *Lancet* 1913, II., p. 859.

* Compare Merck's Reports 1906, 1910 and 1912.

Przedborski, *Berliner klinische Wochenschrift* 1913, No. 43, p. 1987.

(*Ascaris lumbricoides*). He was given three doses of five drops of chenopodium oil at intervals of one hour, followed by a dose of castor oil. On the day of this treatment and on the two following days he passed a large number of worms. A short time after he died from tuberculous meningitis, and the examination of the intestines showed that the child had been entirely freed from worms and their eggs by the oil. Of special importance for the use of chenopodium oil is the fact that in spite of existing nausea and vomiting the child tolerated the drug without further vomiting. W. Schüffner and H. Vervoort also emphasise the fact that chenopodium oil is easily administered, and they found that it is always readily taken when given on sugar. Moreover, the oil is not only a good remedy for ascariasis, but it is also effective in ankylostomiasis. It is more effective than naphthol and thymol, which are also used for this purpose. To expel the parasites the authors gave every two hours three doses of sixteen drops of chenopodium oil on sugar, and two hours after giving the last dose a mixture of 17 grammes of castor oil and 3 grammes of chloroform was administered; the chloroform assists the action of the oil.

Chineonal.

As I already stated in my last year's Report*, chineonal has proved a useful remedy in the treatment of whooping cough. This finding was recently confirmed by Pauli. He is unable to express an opinion as to the value of the remedy in incipient whooping cough, as all the cases which came under treatment were already in the paroxysmal stage. On the other hand, like Armbruster, he found that it is of value in quieting and shortening the attacks. He was able to confirm the observations of Fränkel and Hauptmann that under chineonal treatment the number of attacks is reduced and the vomiting ceases. The author ascribes not only the improvement but also the cures obtained by the use of this remedy to the fact that the patients were not examined from time to time in the policlinic,

Schüffner-Vervoort, Münchener medizinische Wochenschrift 1913, No. 3, p. 129. — Schüffner, Archiv für Tropenhygiene 1912, p. 569.

* Compare Merck's Report 1912, p. 140.

Pauli, Deutsche medizinische Wochenschrift 1913, No. 39, p. 1880.

Armbruster, Merck's Report 1912, p. 141.

Fränkel-Hauptmann, Merck's Report 1912, p. 140.

but that they were kept under constant observation, and that it was thus possible to ensure the proper administration of the drug to the children. Possibly the successful results were also due to the fact that the author continued administering chineonal until the characteristic attacks had disappeared. In some cases in which the use of the remedy was stopped too soon he observed that the attacks became more frequent and more severe. The author states that in no case was it necessary to give narcotics when chineonal was administered, and this statement is worthy of note. Basing on his experience, he says that its absolute harmlessness and its power of enabling the patient to obtain undisturbed sleep are the two chief advantages of chineonal, to which must be added its excellent symptomatic action; it is, therefore, a good remedy for whooping cough. The general health of the children is beneficially influenced in consequence of the good sleep they soon get under its action, they get over the illness better and certainly recover quicker without the occurrence of sequelæ; they are therefore less liable to suffer from complications, in particular tuberculosis. As soon as it is apparent that the drug is well borne it can be given in the same doses as quinine, i. e., one decigramme ($1\frac{1}{2}$ grains) for every year of the child's age.

Chloroform.

Guillon draws attention to the use of chloroform as a tæniacide. He has found it a useful remedy for destroying tapeworms, although it is inferior to thymol*. It can be prescribed as follows:

Chloroform.	4.0
Ol. ricin.	20.0
Pulv. acac.	10.0
Aq. aurant. flor.	20.0
Aq. dest.	ad 150 c. c.

M. Sig.: One quarter to be taken every quarter of an hour.

Of course, it is also possible to administer in the morning, on an empty stomach, 3 to 4 grammes (36—48 min.) of chloroform in water, followed a quarter of an hour later by a

Guillon, Presse médicale 1913, No. 63, p. 644.

* Compare the article on "Thymol" in this Report.

purgative (castor oil or sodium sulphate). Three to four hours later the tapeworm is passed with its head.

W. Hildebrandt discusses the cases of "delayed chloroform poisoning", in which twelve to twenty-four hours after anæsthesia, or after operation, vomiting, acceleration of the pulse, apathy, restlessness, albuminuria, and acetonuria occur, and after one to five days coma followed by death. In a few cases high temperature, jaundice, and delirium have been observed. He arrives at the conclusion that these symptoms are due to the action of chloroform when acute hepatitis is present, and he therefore condemns the use of chloroform as an anæsthetic when an affection of the liver can be diagnosed. In his opinion the use of chloroform in the presence of hepatitis amounts to malpractice, even if an attempt is made to depreciate the danger of the action of chloroform by dietetic measures. In all cases of damage to the parenchyma of the liver he advises the use of ether, or of local or conduction anæsthesia.

Cholalic Acid, Crystalline

Cholalic acid, $C_{24}H_{40}O_5 + H_2O$, occurs in the form of yellowish-white crystals, sparingly soluble in water. Melting point $195^{\circ}C$.

The investigations of K. Glaessner have recently awakened interest in the therapeutic possibilities of cholalic acid*. It is deserving of attention not only in the treatment of obstipation but also in the manifestations of hyperacidity. Glaessner further investigated the action of cholalic acid on pepsin and on the peptic power of the gastric juice, already demonstrated by Hammarsten in 1870, and he came to the conclusion that cholalic acid, and the bile acids, destroy pepsin. After demonstrating this action in vitro the author undertook experiments on man. Cholalic acid was either administered per se in gelatin capsules or in the form of sodium cholate, and he gave two to five doses of 0.1 gramme ($1\frac{1}{2}$ grains) of cholalic acid or 0.2 gramme (3 grains) of sodium cholate in

Hildebrandt, Münchener medizinische Wochenschrift 1913, No. 10, p. 527.

Glaessner, Wiener klinische Wochenschrift 1913, No. 39, p. 1557.

* Compare Merck's Report 1912, p. 419.

Hammarsten, Pflügers Archiv für die gesamte Physiologie 1870, p. 53.

an oily emulsion. These experiments showed that small amounts of cholalic acid are capable of effecting a considerable decrease in the pepsin content of the gastric juice *in vivo*; at the same time the surprising observation was made that the acidity greatly diminished. The reason for this decrease in the acidity of the gastric juice is not quite clear. Glaessner assumes that the bile acids limit the production of hydrochloric acid, although a considerable increase of the gastric juice was observed; this would point to a hypersecretion of secretion poor in hydrochloric acid. These results induced the author to study the action of bile acids in those conditions which he designates as a disposition to ulcerative processes. He distinguishes four groups. The first group includes cases with manifestations of hyperacidity without demonstrable hyperacidity; the second those with hyperacidity without the certain proof of the presence of an ulcer; the third group includes cases of *ulcus ventriculi et duodeni*; and the fourth cases with deficient or lack of normal acidity. His results were as follows:

The cases in group I showed no difference in acidity, but the patients were relieved of their troubles. — In group II in which the majority of cases presented fresh ulcers or erosions, a reduction in the acidity and in the peptic power of the gastric juice was observed in a few instances, in other cases, however, no effect was apparent, and in a few an increase in the values was even observed. Nevertheless, in this group, too, the troubles disappeared in most cases. — In group III, in which the presence of an ulcer was beyond question, a favourable influence on the hyperacidity was noted in several instances. In some cases which were not influenced a subsequent operation demonstrated the presence of a callous or penetrating ulcer. — In the cases included in group IV no effect on the subacid or anacid processes could be observed.

Glaessner believes that the prolonged administration of cholalic acid is likely to yield more satisfactory results than the brief use of this remedy. At least it has now been established that the administration of bile acids brings about a reduction in the acidity and peptic power of the gastric juice, and further that in suitable cases a permanent influence in this direction is possible, and that in many instances the troubles of patients suffering from these conditions disappear and a normal condition is restored.

The test proposed by Mylius for the chemical detection of cholalic acid was modified by J. Ville. As is well known, the addition of iodine to an alcoholic solution of cholalic acid causes the precipitation of blue crystals of iodo-cholalic acid, $(C_{24}H_{40}O_5I)_4 \cdot KI + aq$, if sufficiently diluted with water. Ville suggests the following procedure for applying this test: 20 c.c. of a mixture of 0.5 c.c. of normal solution of iodine and 200 c.c. of a 30 p.c. solution of sodium chloride are added to 2 c.c. of 0.5 p.c. alcoholic solution of cholalic acid. On shaking, a dense precipitate of blue crystalline needles is immediately formed. The conjugated bile acids do not give this test*.

A new preparation containing cholalic acid is issued under the name of "Agobilin".

This is the name applied to a preparation issued in tablet form, each tablet containing 0.088 gramme of strontium cholate, 0.032 gramme of strontium salicylate and 0.04 gramme of phenolphthalein diacetate. The composition of agobilin, and its physiological action, are based upon practical considerations. Recently, Singer and Glässner recommended cholalic acid for stimulating peristalsis, while its action as a chologogue** has been known for some time. Salicylic acid possesses a certain amount of analgesic action, which, according to Th. Runck, is displayed even by the small doses present in agobilin. Strontium is said to allay inflammation and in combination with cholalic acid is said to considerably enhance the therapeutic value of the latter. The phenolphthalein diacetate acts as a primary stimulant to peristalsis.

The results recorded by Runck show that agobilin is a valuable remedy for the successful treatment of affections of the biliary system. Except during the stage of an acute attack in which the use of morphine as an anodyne cannot be dis-

Mylius, *Berichte der deutschen chemischen Gesellschaft Berlin* 1887, Vol. 20, p. 683.

Ville, *Bulletin de la société chimique de France* 1913, Vol. 13, p. 866.

* Compare Merck's *Reagenzien-Verzeichnis* 1913, p. 253.

Singer-Glässner, *Merck's Report* 1912, p. 419.

** Compare Hammarsten, *Lehrbuch der physiologischen Chemie* 1904, p. 260. — E. Stadelmann, *Deutsche medizinische Wochenschrift* 1896, No. 49, p. 785.

Runck, *Allgemeine medizinische Zentralzeitung* 1913, No. 20, p. 237.

pensed with, the author always succeeded with the help of agobilin in bringing about a condition of latency. The transition to a condition of free intervals and rest often took place so readily as to appear a matter of course. It is true, the attacks recurred, but they became less frequent, shorter and milder. In some of his cases a condition of latency set in following a short treatment with agobilin, while others required a prolonged treatment. Cases of chronic cholecystitis associated with fever, jaundice and colic which suggested the presence of an empyema or a stricture of the cystic duct required permanent treatment. Runck does not believe that agobilin treatment is indicated in these cases, although it frequently displayed a beneficial action on the symptoms. On the other hand, the author draws attention to the fact that up to the present no operation has been required in about 150 cases treated with agobilin, even in the severe cases included in this number. The beneficial action of agobilin was usually apparent in the comparatively rapid disappearance of the swelling of the liver, if present, in the disappearance of the feeling of fulness in the abdomen and in a decrease in the feeling of pressure in the region of the liver. As agobilin does not produce any particularly severe attacks, the author assumes that the antiphlogistic effect of strontium, the slightly analgesic action of salicylic acid and the primary evacuating effect of phenolphthalein diacetate successfully contribute to promote the display of the cholagogue action of cholalic acid. He therefore recommends the use of this remedy for the treatment and prophylaxis of gall-stone diseases and associated conditions. He administered at the commencement of treatment two tablets twice a day, two to be taken immediately after breakfast and two about twelve hours later, e. g., at 8 a. m. and again at 8 p. m. By this means it is possible to effect the simultaneous display of the action produced by agobilin with the physiological maximum secretion of bile.

L. Seiler administered agobilin only when the acute attack was on the decline, and gave one to three tablets three times a day. He is of opinion that sufferers from gall-stones might be benefited by being put on a regular course of two to three tablets of agobilin twice weekly. However, in cases which from the beginning require operative

treatment, such as acute inflammatory processes which point to the presence of severe infection, chronic inflammatory processes with septic symptoms, chronic closure of the cystic duct or suspected carcinoma, should not be submitted to agobilin treatment.

The chemical examination of the constituents of agobilin has been discussed by R. Werner and H. Runne, and for details of their method the original paper should be consulted.

Cholesterin.

The property of cholesterin* of neutralising hæmolytic processes, mentioned by F. Ransom and recently confirmed by G. Jahnson-Blohm, is likely to find a useful application in therapeutics. Using this fact as a basis, J. Pringsheim tried the use of cholesterin in paroxysmal hæmoglobinuria, in which hæmolytic processes play a certain part. In order to obtain the absorption of larger amounts of cholesterin the author gave intramuscular injections of a 10 p. c. emulsion. The injections are rather painful and sometimes accompanied by a slight rise of temperature, however, according to Pringsheim's investigations they are rapidly absorbed. In order to throw some light on the effect of cholesterin in paroxysmal hæmoglobinuria, attacks were produced from time to time in a patient by the use of a cold foot-bath, and their severity was judged by the duration and degree of the resulting hæmoglobinuria in the urine. In the course of eleven days the patient was given five intramuscular injections of 0.5 c.c. of the 10 p. c. cholesterin emulsion, with the result that on the eleventh day the irritation produced by the cold caused only a very slight elimination of blood in the urine, whereas formerly it gave rise to severe attacks. Eight days after the last injection of cholesterin it was possible again to produce attacks similar in severity to those which occurred before treatment. Therefore, the conclusion may be drawn that cholesterin is

Werner-Runne, Pharmazeutische Zentrallhalle 1913, No. 25, p. 613.

* Compare Serono, *Funzione biologica e terapeutica della colessterina*. *Rassegna di clinica e terapia*, March 15, 1913.

Ransom, *Deutsche medizinische Wochenschrift* 1901, No. 13, p. 194.

Jahnson-Blohm, *Zeitschrift für physiologische Chemie* 1913, Vol. 85, p. 59.

Pringsheim, *Medizinische Klinik* 1913, No. 7, p. 254. — *Semaine médicale* 1913, No. 10, p. 114.

capable of cutting short an attack of hæmoglobinuria. The mechanism of the action of cholesterin, however, still awaits elucidation.

C. Cantieri describes a case of splenic anæmia in a child, in which cholesterin proved very effective. The author did not use pure cholesterin, but the palmitin and olein ester of cholesterin which is issued in an oily solution under the name of "choleol" in ampoules of 1 c.c. He injected it in series of several subcutaneous injections, daily or at longer intervals. This treatment led to an appreciable reduction of the enlargement of the spleen and to an improvement of the child's general condition.

As is well known, Grimm, Külz and Seiffert found cholesterin a useful remedy for blackwater fever. H. Werner, however, was unable to confirm this, and he reports two cases in which doses of 3 grammes (45 grains) of cholesterin in olive oil, in conjunction with the administration of quinine, did not increase the tolerance for quinine, and the fever and hæmoglobinuria still persisted for some days.

The determination and quantitative estimation of cholesterin in organic fluids has of late years assumed increased importance in physiology, as by this means it is possible to gauge the importance of cholesterin metabolism in the organism*. Papers on this subject have been published by O. Weltmann, W. Autenrieth and A. Funk, E. Schreiber and J. Lifschütz.

For those cases in which absolute quantitative accuracy is not aimed at and where results are required merely for comparison, Weltmann has elaborated a colorimetric method which permits the estimation of the cholesterin content of blood. It is based upon Salkowski's* cholesterin test, and is conducted as follows:

Cantieri, Wiener klinische Wochenschrift 1913, No. 48, p. 1978.

Grimm, Külz, Seiffert, Merck's Report 1910, p. 144.

Werner, Archiv für Schiffs- und Tropenhygiene 1913, Vol. 17, p. 8.

* Compare D. Klinkert, Tijdschrift voor Geneeskunde 1912, No. 25 and L. Wacker and W. Hueck, Archiv für experimentelle Pathologie 1913, Vol. 71, p. 373.

Weltmann, Wiener klinische Wochenschrift 1913, No. 22, p. 874.

Autenrieth-Funk, Münchener medizinische Wochenschrift 1913, No. 23, p. 1243.

Schreiber, ibidem 1913, No. 36, p. 2001.

Lifschütz, Biochemische Zeitschrift 1913, Vol. 54, p. 212.

1 c. c. of serum is introduced by means of a capillary pipette into a long-necked measuring flask of 50 c. c. capacity and a mixture of 10 c. c. of concentrated sulphuric acid and 10 c. c. of chloroform is added. The mixture is then well shaken for two minutes, the glass stopper being lifted at the beginning. The whole is kept in the dark on ice for twenty-four hours, and the mixture is then transferred into a test-tube of a prescribed diameter the glass wall of which possesses a definite thickness; it is closed with an indiarubber stopper. The result of the reaction can now be read, i.e., the red tint of the chloroformic layer is examined by the aid of a simple apparatus the principal part of which is the ruby glass prism of Fleischl's hæmometer. On the whole, the tints correspond very well with the glass prism. Should the chloroformic layer still have a yellowish-red colour at the expiration of the twenty-four hours, all that is necessary is to allow it to stand for some time in diffused light whereby the transformation into the red colouring matter quickly takes place. Although this method may suffice for many clinical purposes, however, for exact physiological experiments recourse must be had to the estimation of cholesterin by means of digitonin according to Windaus's method, notwithstanding that, under certain circumstances, a larger quantity of material for examination as well as special training in the application of this method of analysis are required. Nevertheless, Autenrieth and Funk have investigated the more simple colorimetric method of estimating cholesterin. They start from Lieberman-Burchard's test**, which depends upon the production of a red colour by the addition of sulphuric acid to a solution of cholesterin in chloroform and acetic anhydride, which gradually changes to blue, bluish-green and finally to green. The cholesterin esters and oxycholesterin give the same reaction. To obtain the same tints for making comparisons special precautions must be observed in carrying out the test. For details of the method the original work should be consulted; however, it may be mentioned that this method differs from the one described above chiefly in that the cholesterin is extracted with ether or chloroform from the material to be examined,

* Compare Merck's Reagenzien-Verzeichnis 1913, p. 312.

** Compare Burchard's test for Cholesterin in Merck's Reagenzien-Verzeichnis 1913, p. 54.

and is estimated in the chloroformic solution after the addition of definite amounts of acetic anhydride and sulphuric acid in the colorimeter of Autenrieth-Königsberger.

In succession to the statements by Autenrieth and Funk Schreiber draws attention to the fact that oxysterin is not precipitated by digitonin*, but that, like sterin, it can be estimated colorimetrically according to the method of both authors. He expresses the belief that oxysterin is a substance which is physiologically important and therefore suggests carrying out its quantitative estimation by extracting the total sterin bodies from the material to be examined, the sterin is precipitated by digitonin, whereupon the oxysterin present in the remaining solution is determined colorimetrically by the method described above. On the other hand, Lifschütz states that oxysterin as well as sterin are precipitated by Windaus's method, and for the determination of both substances, when present together, the author has elaborated a method based on the use of the spectroscope. (For details the original work should be consulted.)

M. Bürger and Beumer adopt the following method for the estimation of sterin and sterin esters. The dried material to be examined is extracted with alcohol and chloroform, and the mixture of sterin substances thus obtained is weighed after evaporation of the solvent. The residue is dissolved in ether and purified with acetone. After evaporation of the ether the residue is dissolved in alcohol and the resulting solution is divided into two parts. In one portion the sterin is precipitated with digitonin by Windaus's method; in the other portion the sterin is first hydrolysed and then precipitated with digitonin. The difference between both determinations indicates the amount of sterin set free from the esters.

* This statement, according to J. Lifschütz (Münchener medizinische Wochenschrift 1913, No. 42, p. 2346), is inaccurate. Oxysterin and sterin in alcoholic solution are both almost entirely precipitated by digitonin. Therefore, Schreiber's method does not permit the quantitative estimation by colorimetric means of oxysterin in the presence of sterin, nor is it possible by its means to separate quantitatively oxysterin from sterin by precipitation with digitonin.

Bürger-Beumer, Berliner klinische Wochenschrift 1913, No. 3, p. 113.

Choline.

During the past year no contributions to medical literature of interest to general practitioners were published dealing with choline and its use in malignant tumours. On the other hand, N. Trinkler and J. Sellei were able to confirm the value of choline and of preparations of choline, as described by Werner and Szécsi. In some cases Sellei succeeded in obtaining surprising results with this preparation.

The observations of G. Cavina and L. Launoy throw some light upon the mode of action of choline. According to Cavina the intravenous injection of choline causes a demonstrable lesion of the liver cells, apparent in a reduction of the glycogen. Launoy was able to prove that the increased pancreatic secretion caused by the intravenous injection of choline is due to its effect as a quaternary base.

Another possible therapeutic use for choline has been found by H. Mehler and L. Ascher, and is based upon the observations of Deyke and Much that choline is capable of dissolving tubercle bacilli. Whereas Deyke used this finding as a basis for his attempts to prepare an effective tuberculin by the aid of choline, the above mentioned authors tried the direct incorporation of choline in order to effect a kind of bacteriolysis of the tubercle bacilli in the organism. For this purpose they used the boro-choline suggested by Werner, which is issued in 10 p.c. solution under the name of "enzytol".

The authors' investigations show that boro-choline can be introduced in comparatively large doses into the blood current without harm, even in tuberculotics; it produces a typical reaction in cases of acute tuberculosis. For injection a 1 or 2 p.c. solution of boro-choline in normal saline solution was used, of which at first 1 c.c., and later up to 10 c.c., were injected or infused. The patients did not complain of any disagreeable sensations as long as doses not exceeding 0.05

Trinkler, *Zentralblatt für Chirurgie* 1913, No. 7, p. 242.

Sellei, *Zeitschrift für Chemotherapie* 1913, p. 406.

Werner-Szécsi, *Merck's Report* 1912, p. 144.

Cavina, *Riforma medica* 1913, No. 4.

Launoy, *Journal de physiologie et de pathologie générale* 1913, Vol. 15, p. 280.

Mehler-Ascher, *Münchener medizinische Wochenschrift* 1913, No. 14, p. 748.

Deyke-Much, *ibidem* 1909, No. 39, p. 1985.

gramme ($\frac{3}{4}$ grain) of boro-choline were injected; however, if the dose is increased to 0.2 or 0.25 gramme (3—4 grains), or if a more concentrated solution is used (2 p. c.), a very characteristic symptom-complex is produced which, as choline effect, has already been described by pharmacologists. Before making use of boro-choline care must be taken to see that the preparation has not undergone partial decomposition, apparent by a smell of trimethylamine, otherwise it may produce attacks of dyspnoea. In surgical tuberculosis an increase of the serous wound secretion was observed already on the day after the first injection of boro-choline, and occurred after each subsequent injection. At the same time healthy and fresh-looking granulations were formed, large wound cavities filled within a surprisingly short time and healed up readily without the formation of fistulas. Coincident with the objective improvement in the appearance of the wound there is also an improvement in the patient's condition; the cough is relieved, the appetite improves and there is an increase in weight, while sleep is improved. In most cases, too, the pulse rate is slowed and returns to normal. In febrile tuberculosics the authors proceeded very cautiously and tentatively in the dosage of the preparation. They commenced with a dose of 0.01 gramme ($\frac{1}{6}$ grain) of boro-choline, as they had observed a very febrile reaction to follow an injection of 0.06 gramme (1 grain) in a case of acute tuberculosis. Of interest is the observation that the administration of a total amount of 1.5 grammes (24 grains) of boro-choline frequently caused extensive destruction of the tubercle bacilli in the sputum. From the foregoing remarks it is apparent that the further trial of boro-choline in tuberculosis is justified. In a subsequent publication* the authors state that a combination of boro-choline and copper is still more efficacious than boro-choline per se.

Coagulin.

For the preparation of a new styptic, the so-called "coagulin Kocher-Fonio", A. Fonio used as a basis the fact that in the process of decomposition of the blood-plates present in blood a substance is set free which, by acting like a ferment, causes the precipitation of fibrin and thereby produces coagula-

* Münchener medizinische Wochenschrift 1913, No. 19, p. 1041.
Fonio, Korrespondenzblatt für Schweizer Ärzte 1913, No. 13—15.

tion of the blood. It must be assumed that the other factors which are required for this purpose are present in the blood. To produce his preparation the author employed the so-called thrombozym of Nolf, which can be obtained from the blood-plates and can be heated to 100° C. without decomposition. Therefore, this preparation, to which he has given the name of "coagulin", can be sterilized and put up in ampoules. It is also issued in powder form, which must be dissolved and sterilized before use. The hæmostatic action of this preparation was tested by the author in practice. With regard to his theoretical considerations the original paper should be consulted; in the following remarks the mode of use of, and the indications for, the new preparation are given.

In herniotomies, appendicectomies, laparotomies, etc., according to Fonio's directions, all the bleeding vessels are first of all compressed with clamp forceps in order not to delay the prompt performance of the operation. Instead of ligating, the forceps are then removed and coagulin is poured upon the part which was compressed. Under this treatment slight bleeding from arteries is immediately arrested; in the presence of more profuse hæmorrhage brief compression with a finger is required. To prevent secondary hæmorrhage the whole wound is then treated with coagulin. In strumectomies only the hæmorrhages in the skin, on the fasciæ and from the muscles are treated in this way. After ligation of the other clamps the wound is cleansed with water, dried and irrigated with coagulin, whereupon the clamps applied to the skin, fasciæ and muscles are removed, the wound filled with normal saline solution and closed without drainage. In operations where there is greater loss of blood, such as trepanations and operations on bones, and in which larger superficial wounds are produced, to obtain a more rapid thrombus formation the blood should be quickly wiped away and the bleeding surface immediately irrigated with coagulin, lightly applying a gauze tampon. If necessary, this procedure is repeated until the bleeding is checked. The wound can then be closed without drainage. To prevent the formation of cavities they are filled with normal saline solution. A compression bandage is not required, it is quite sufficient to apply a protective dressing of strips of xeroform gauze and collodion. Arteries of medium size must be compressed with the finger until the thrombus adheres, so that it is not washed away by the blood. To

ensure a successful result with coagulin treatment the preparation must come into contact with the bleeding part so that the bleeding lumen of the vessel can be closed by the thrombus.

Cocaine Hydrochloride.

E. Fuld reiterates the value of cocaine in the treatment of nervous diarrhœa, to which he has already drawn attention in a previous communication*. In the author's opinion most diarrhœas, including the great majority of cases of intestinal catarrh, are due to a nervous basis, and in consequence of the existence of a gastro-intestinal reflex mechanism normal defæcation as well as obstipation are also due to the same cause. Cocaine prevents the occurrence of the reflex excitability of the gastric mucous membrane and by its use the irritation of the stomach produced by the ingestion of food is suppressed, without causing any disturbances of nutrition. The author has obtained very good results with his method in a large number of instances, including cases of achylia. As was stated in my last year's Annual Report, Fuld at first administered cocaine in combination with codeine, now, however, he uses cocaine by itself. The patient is ordered to take ten drops of a 3 p. c. solution of cocaine hydrochloride (in water or peppermint water), mixed with a little water, ten minutes before meals. To obtain a permanent success it is usually sufficient to continue this treatment for a few days only.

An important contribution on local anæsthesia has been published by A. Herzfeld. He states that alcohol is an excellent drug for preventing acute cocaine intoxication, such as may occur particularly in females who exhibit an idiosyncrasy to cocaine. The author gives to every patient without exception a large dose — 25 to 50 c.c. — of whisky or brandy by mouth ten to thirty minutes before the first injection of cocaine. To women and children it is given in sugar and water. With this treatment he has never had a single unpleasant experience in the course of four years in inducing local anæsthesia by cocaine. Herzfeld's suggestion is worthy of trial especially in dental work.

* Merck's Report 1912, p. 150.

Fuld, Münchener medizinische Wochenschrift 1913, No. 21, p. 1183.

— Compare also Semaine médicale 1912, No. 35, p. 409.

Herzfeld, Zentralblatt für Chirurgie 1913, No. 44, p. 1705.

Cozette obtained noteworthy results with cocaine in the treatment of acute laminitis in horses. He injected into the animals 10 c. c. of a 3 p. c. solution of cocaine hydrochloride, or, in order to increase the anæsthetic action, he injected a solution of 0.3 gramme of cocaine hydrochloride and 1 c. c. of adrenalin in 10 c. c. of normal saline solution into the plantar nerves. Already after the first injection the animals were able to rise. One horse was cured in a fortnight, two others could be led into the water already on the third day and were also cured after twelve days.

Codeonal.

A pharmacological study of codeonal was published by G. Dietz as the result of experiments on large and small animals. He found that doses of 0.15—0.17 gramme of codeonal per kilogramme of rabbit or dog cause deep sleep from which the animals were roused with difficulty; the administration of larger amounts caused sleep from which they could not be roused at all. Sleep was induced in about one hour to one hour and a half and had fully developed after six hours, and lasted in all about fourteen hours. The fall in temperature observed never on an average exceeded 0.5° C. In addition, an increase in the pulse rate and a decrease in the respiratory rate were observed. No disturbance of appetite was noted; on the other hand, conditions of paralysis lasting for some time were observed. In horses a dose of 20 grammes of codeonal caused a sleepy condition without any injurious secondary effects. The author states that the drug is not suited to ruminants.

The value of codeonal in the treatment of insomnia is reported upon by Th. Mann, Bönning, Marcantoni, Leva and M. Lomnitz. In close upon one hundred cases of insomnia Mann gave the remedy, in doses of one to three tablets, and obtained on the whole very satisfactory results.

Cozette, *Berliner tierärztliche Wochenschrift* 1913, No. 5, p. 81.

Dietz, *Dissertation* Giessen 1913.

* Compare Merck's Report 1912.

Mann, *Münchener medizinische Wochenschrift* 1913, No. 9, p. 474.

Bönning, *Berliner klinische Wochenschrift* 1913, No. 29, p. 1353.

Marcantoni, *Gazzetta degli ospedali e delle cliniche* 1913, No. 2.

Leva, *Medizinische Klinik* 1913, No. 23, p. 911.

Lomnitz, *Halbmonatsschrift für soziale Hygiene und praktische Medizin* 1913, No. 7 and *Medizinische Reform* 1913, p. 134.

The effect usually set in after three quarters of an hour and lasted about seven hours. In various affections of the respiratory tract it allayed the troublesome cough and caused the respiration to become deeper and more regular; in affections of the nervous system its action was reliable only in milder cases.

Bönning employed codeonal with satisfactory, and in some instances with very good results, as a hypnotic in insomnia due to neurasthenia, troubles during the climacteric, hepatic colic, erections, pollutions, nightly cough, over-fatigue, etc. He found that the remedy displays a good sedative action, does not otherwise affect the general health and is usually reliable; its action is greater in women than in men.

Marcantoni considers codeonal a good remedy in neurasthenia, and in hysteria associated with cardiac and gastric disturbances, and also in cardialgia, gastralgia, flatulence and conditions of fear.

In psychoses and neuropsychoses accompanied by general motor excitement and restlessness and severe emotional conditions of excitation, Leva found that the sedative effect of codeonal is rarely adequate, as in these cases the narcotic action is evidently insufficient. On the other hand, it is very useful as a hypnotic in conditions of mild general nervous excitement and exhaustion, and also in organic affection of the nerves associated with bodily pains.

Lomnitz also reports good results with codeonal in sleeplessness due to pulmonary tuberculosis, nervousness, and depression. It also proved useful in tabetic pains. E. Bergeat, too, found that it displayed a good sedative and hypnotic action in various painful diseases of the teeth, and also in the pains following difficult extractions. In these cases two or three tablets are given for a dose. The administration of codeonal before operations is very useful in calming the patients.

Colchicine.

As colchicine*, which is used in the treatment of acute attacks of gout, is a comparatively poisonous substance, the derivatives of colchicine prepared and described by Zeisel,

Bergeat, *Monatsschrift für Zahnheilkunde* 1913, No. 5, p. 336.

* Compare Merck's Report 1908 and 1909.

Zeisel, *Wiener Monatshefte für Chemie* 1883, Vol. 4, p. 162; 1886,

Vol. 7, p. 557 and 1888, Vol. 9, p. 1 and 865.

Paschkis and Windaus are not devoid of therapeutic interest. For this reason H. Fühner undertook their pharmacological investigation in order to prepare the way for their use in therapeutics. He investigated the action of colchicine, trimethylcolchicinic acid, trimethylcolchicinic acid methyl ether, N-benzoyltrimethylcolchicinic acid methyl ether, N-benzoylcolchicinic acid anhydride and oxycolchicine, and obtained the following results:

Colchicine, in which only one enolmethoxyl group of colchicine* is hydrolysed, possesses a far weaker action than its methyl ether, i. e., colchicine. With the further dissociation of the acetyl residue from the amino-group, which leads to the formation of trimethylcolchicinic acid (Zeisel), the activity, compared with colchicine, agains increases. The toxicity still more closely approaches that of colchicine itself if the methoxyl group originally present in colchicine is re-introduced through methylation. The benzylation of this product yields a substance which differs from colchicine only in that it contains a benzoyl group in the place of the acetyl group. In experiments on cats it was found that the action on the stomach and intestines displayed by this derivative was about ten times weaker than that of colchicine. An internal acid anhydride produced by further decomposition by means of oxidation and benzylation in the amino group, when given in large doses still exhibited the colchicine action on the intestines. The most interesting of the substances investigated by Fühner

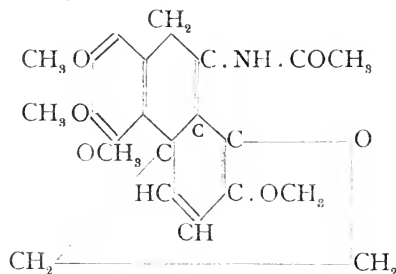
Paschkis, Wiener medizinische Jahrbücher 1883, p. 257 and 1888, p. 569.

Windaus, Sitzungsberichte der Heidelberger Akademie der Wissenschaften, Mathemat.-naturwiss. Klasse 1910, 1—7, and 1911, 1—27.

— Jahresberichte der Pharmazie 1911, p. 195.

Fühner, Archiv für experimentelle Pathologie 1913, Vol. 72, p. 228.

* According to Fühner, colchicine very probably has the following structural formula:



is oxycolchicine, especially in relation to oxydicolchicine (Jacobi). In cold-blooded animals (frogs) it has a convulsive action, and smaller doses are required to produce this effect than is the case with oxydicolchicine; on the other hand, it does not produce any action in mammals, even in large doses. Clinical trials are necessary to demonstrate whether colchicine may be substituted by any of these, to some extent less toxic, substances in the treatment of gout.

Colpitol.

K. von Sande describes an immunising bacterial preparation obtained from the streptococcus of Ostertag; it is issued under the name of "colpitol" and occurs as a yellowish-white powder. It is intended for use as a local immunising agent in the treatment of infectious vaginal catarrh, and the author's trials showed that it yielded good results in this condition. In order to establish its harmlessness he introduced the preparation into the vagina of various animals such as rabbits, guinea-pigs, sheep and mares, leaving it in situ for several days, and he never observed any signs of irritation whatever either on the uninjured or on the purposely injured mucous membrane of the vagina. On the contrary, the preparation exerted a beneficial influence on the injuries. The bacteriological investigation of colpitol showed that it was free from living germs.

Colpitol is applied in the form of a powder to the inflamed mucous membrane in the region of the clitoris. It must be carefully applied as it only acts where it comes in direct contact with the mucous membrane. Göhler also expresses a favourable opinion regarding the value of this new preparation. He obtained a cure in 30 p. c. of the cases treated by it, while an improvement was observed in almost all of the remaining cases.

Contraluesin.

Contraluesin is the name applied by E. Richter to an extremely fine suspension of metallic mercury in an aqueous solution of salts themselves possessing antiluetic properties.

Sande, Berliner tierärztliche Wochenschrift 1913, No. 20, p. 365.

Göhler, Zentralblatt für Bakteriologie 1912, Vol. 65, No. 8.

Richter, Dermatologische Wochenschrift 1912, Vol. 55, No. 39, p. 1218.

The author does not enter into details regarding these salts and the amounts present, he merely states that the solution contains sozoiodol-quinine, salicylates, corrosive sublimate and arsenic. Therefore, contraluesin, which is issued in ampoules of 1 c. c. = 0.15 gramme of mercury, combines three actions: an acute antiluetic (corrosive sublimate and arsenic; a chronic antiluetic (mercury); and a general bactericidal action (sozoiodol-quinine and the salicylates). Contraluesin is injected intramuscularly into the buttocks, after cleansing the site of injection with spirit of soap and painting with tincture of iodine. Richter ascribes the value of this preparation to the fine division of the mercury in the aqueous solution. The mercury is said to be in a state of subdivision finer than the size of streptococci, so that it is capable of being quickly absorbed. Absorption is all the more complete since the metal is suspended in water and not in oil, which is known to retard absorption. A further advantage of this fine division is, according to Richter, the fact that in spite of the high specific gravity of the metal it remains suspended in the solution for several hours. The author established the innocuousness of the preparation by experiments on animals and upon himself.

G. Schourp tried contraluesin in 88 cases of syphilis and found that it is very effective and does not cause any harm. It acts very quickly and after a few injections of 0.1 to 0.15 gramme of mercury displays a permanent effect.

E. Klausner also expresses a very favourable opinion upon the value of contraluesin. In his experience the injections are practically painless, do not produce infiltrations and stomatitis does not occur if the patients observe the prescribed hygiene of the mouth. For this purpose Richter prescribes gargling with a solution of hydrogen peroxide to which is added as much as will go on the point of a knife of a mixture of 55 grammes (2 oz) of sodium bicarbonate, 5 grammes (75 grains) of sodium sulphate, 5 grammes (75 grains) of sodium salicylate and 0.1 gramme ($1\frac{1}{2}$ grains) of menthol.

Convallaria Majalis.

A brief review of the active principles and the use of Convallaria in the treatment of heart diseases was given in

Schourp, Dermatologisches Zentralblatt 1912, Vol. 16, No. 3.

Klausner, Münchener medizinische Wochenschrift 1913, No. 2, p. 62.

my Annual Report for the year 1911. Recently A. Strubell has directed attention to this cardiac tonic in the assumption that it might prove useful in mild forms of heart disease, such as occur in robust, apparently quite healthy persons, and occasionally in patients suffering from chronic heart diseases in the intervals between severe attacks. For his experiments he made use of a preparation introduced by Boruttau and known under the name of "Kardiotonin", a combination of extract of *Convallaria* freed from convallamarin and physiologically standardised, with caffeine. Of this preparation 0.2 c. c. represent the active, and 0.5—0.6 c. c. the lethal dose per kilogramme of rabbit. For a therapeutic initial dose 1 c. c. is given by mouth; this amount contains 0.025 gramme of caffeine, held in solution by 0.03 gramme of sodium benzoate. According to Bickel and Pawlow the action of this preparation is principally due to slowing of the heart's action, consisting in an increase of the heart's phase and also of the period of cardiac rest and thus resulting in effecting a favourable influence on the cardiac function. For this reason the authors recommend it in slight compensatory disturbances, in which digitalis and strophanthus are usually not given. Strubell gives more definite indications for its use. The results of his experiments show that it acts rather upon the cardiac nerves than upon the muscular apparatus of the heart and the bundle of His. The evident slowing of the pulse and the decrease in subjective troubles referable to the heart, according to the author, point to the utility of kardiotonin in the treatment of mild and moderate cardiac neuroses often accompanied only by subjective troubles, chloroses and anæmias associated with diseases of the heart, incipient thyrotoxic cardiac affections, and mild pseudo-anginal and anginal conditions in angio-sclerosis and arterio-sclerosis. For a single dose Strubell gave 1 c. c. of kardiotonin internally.

Copper, Colloidal

Among the newer remedies for cancer colloidal copper appears to claim increasing interest, and during the past year this preparation has been studied by a number of investi-

gators, including L. Loeb, C. B. McClurg, W. O. Sweek, Moyer, S. Fleischer, W. E. Leighton, O. Ishii, Wolze, A. Pagenstecher, H. Roziès, A. J. Gelarie, J. Gaube du Gers, H. Chabanier, L. Rollin, P. Jacques and R. Weil.

Gaube, in succession to a former contribution*, reports upon fifty cases in which he used cuprase, a colloidal copper containing albumin. He injected at intervals of several days the contents of one ampoule (of 5 c. c. = 0.00121 gramme of copper), subcutaneously or intramuscularly, and he found that the preparation did not cause any, or only a very slight, general reaction and did not produce any local symptoms of irritation, and on the whole it was well borne. It is said to have a selective action on cancer cells, extending to all forms of cancer, in consequence of which it arrests carcinomatous proliferations, absorbs glandular swellings and causes ulcers to cicatrize. Even in comparatively advanced cases the preparation is said to display a curative, analgesic, tonic, and hæmostatic action; further, it improves the appetite and exerts a beneficial influence on the general condition.

Loeb and his collaborators were also able to observe a retarding influence of cuprase and of some other copper preparations (copper casein) on mouse tumours, which disappeared on stopping the preparation. They injected cuprase intravenously six times a week into cancer patients. After the use of larger doses they observed shortly after the injection rigor and a rise of temperature up to 38° or 39° C., and these symptoms were sometimes accompanied by acceleration of the pulse. These phenomena diminished on continuing the treatment. The action of the injections manifested itself in

Loeb, McClurg, Sweek, Fleischer, Leighton, Ishii, *Interstate Medical Journal* 1912, December and 1913, January. — *Prescriber* 1913, Vol. 7, p. 181.

Wolze-Pagenstecher, *Münchener medizinische Wochenschrift* 1913, No. 19, p. 1036.

Roziès, *Gazette des Hôpitaux* 1913, Vol. 86, p. 327.

Gelarie, *British Medical Journal* 1913, II, p. 222.

Gaube, *La cuprase et le cancer* — 50 observations nouvelles. Paris 1913, Jules Roussel.

Chabanier-Rollin, *Presse médicale* 1913, No. 11, p. 102.

Jacques, *Scalpel et Liège médicale* 1913, Vol. 66, p. 176.

Weil, *Journal of the American Medical Association* 1913, 27th September.

* Compare Merck's Report 1912, p. 156.

a hyperæmia of the tissue surrounding the tumour, and in increased secretion in the case of ulcerated tumours. This was followed by a gradual decrease in the size of the tumour and recovery. The author obtained a cure in two out of eight inoperable cases. On the other hand, in extensive metastases the result was negative or only very slight, and the same observation was made by other investigators. Therefore, cases presenting rapid formation of metastases and advanced cachexia should not be treated with cuprase, as it is useless to expect a successful result in these cases.

Wolze and Pagenstecher report very favourably on the action of cuprase. They succeeded in bringing about a condition of latency by the combined use of cuprase and X ray treatment in a case diagnosed histologically as sarcoma. In all eight injections of 5 c. c. of cuprase were made, i. e., a total amount of 0.00968 gramme of copper was injected in the course of seven weeks. The tumour decreased in size and the general condition improved. Although this result cannot be described as a cure, still the authors ascribe a part of the success obtained to the use of cuprase and X ray treatment.

On the other hand, Roziès' results are less encouraging. He reports four cases of inoperable carcinoma of the rectum, uterus, and pharynx, in which the contents (5 c. c.) of an ampoule of cuprase were injected intramuscularly at intervals of four days. With the exception of pains lasting for some hours in the site of injection, no unwelcome side effects were observed; in one case the pain in the carcinoma was relieved. However, there were no signs whatever pointing to a beneficial influence on the offensive discharge nor any evidence of cessation or involution. In twelve cases of malignant tumours Weil was unable to observe any therapeutic effect whatever of colloidal copper.

Chabanier and Rollin describe the effect of the preparation on the blood picture. They state that the injections of cuprase at first cause a decrease in the hæmoglobin content and in the number of red blood corpuscles, but after seven or eight days the blood again becomes normal. The number of leucocytes decreases immediately after an injection, but increases enormously after one or two days — i. e., is doubled. The number of leucocytes reaches its maximum on the third or fourth day, and then gradually returns to normal.

Pulmonary tuberculosis offers a further indication for colloidal copper. According to Damask intravenous injections of electrocuprol effect fairly rapid defervescence which is maintained for some time, and is accompanied by a marked tonic action. However, this effect is displayed only in mixed infections, and is without influence on the physical condition of the lungs. Therefore, treatment with electrocuprol is chiefly indicated in hyperpyretic cases of pulmonary tuberculosis. The author injected 1 or 2 c. c. of electrocuprol and repeated the injection every second or third day. If the first injections were well borne, Damask gradually increased the dose up to 5 c. c.; to produce complete apyrexia three to twelve injections were required.

For experiments on mouse tumours Gelaire used a copper sol prepared according to Bredig's method, and with it obtained a cure in 6.3 p. c., a decrease in the size of the tumour in 12.5 p. c., enlargement in 31 p. c., and in 50 p. c. a stillstand in development. On section it was found that the tumours showed distinct degeneration.

Copper Salts (Cupric Chloride, Copper Ammonio-Sulphate, Potassio-Cupric Tartrate).

The chemotherapeutic investigations undertaken by Linden with copper salts induced St. Pekanovich to try cupric chloride and potassio-cupric tartrate in pulmonary tuberculosis. Cupric chloride, $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, occurs as a green, very deliquescent crystalline mass, freely soluble in water and in alcohol. Potassio-cupric tartrate, $\text{CuK}_2(\text{C}_4\text{H}_4\text{O}_6)_2$, forms blue scales readily soluble in water.

The subcutaneous and intramuscular injection of copper salts caused such severe pain and necroses that the author gave up this method in favour of intravenous injection. At first he administered the salts in 1 p. c., later in 2 p. c. solution, in physiological salt solution in doses of 0.5 to 2 c. c. The patient was given an initial injection of 0.5 c. c. of the 1 p. c. solution, gradually passing on to larger doses. With proper technique the injections are not painful, and no in-

Damask, Wiener medizinische Wochenschrift 1913, No. 19, p. 1185.

Linden, Beiträge zur Klinik der Tuberkulose, Vol. 23, No. 2. — Zentralblatt für die gesamte Arzneimittellkunde 1912, No. 8/9, p. 401.

Pekanovich, Deutsche medizinische Wochenschrift 1913, No. 28, p. 1352.

filtrations or thromboses were observed. To enhance the copper action the author also employed tuberculin, which was given sixteen to twenty-four hours before the injection of the copper salt. For this treatment Pekanovich selected patients in the second stage as in these the action of the drug can best be controlled, and also febrile cases in order to study the effect on the fever. In eighteen patients in whom this treatment was tried it was found that the copper salts had no effect whatever on the temperature curve whichever copper salt was given. The organism quickly became habituated to the copper so that in time even large doses no longer produced any reaction. Thus, at first the temperature falls slightly after the injection, but later there is no response. Nor were the other symptoms of pulmonary tuberculosis influenced in any way. In no case was there any striking improvement in the appetite or a gain in weight, or a decrease in the expectoration. The slight improvement which was observed in a few cases is ascribed by the author to the hygienic and dietetic measures adopted. Moreover, in several cases the condition grew worse.

No better were the results on using the copper salts in the form of ointments. Inunction with a 1.5 p. c. ointment even caused painful inflammatory symptoms, so that its use had to be abandoned.

A. J. Gelarie made experiments with copper ammonio-sulphate, $\text{CuSO}_4 \cdot 4\text{NH}_3 \cdot \text{H}_2\text{O}$, on mouse tumours; he prepared this compound himself according to a special formula. It was dissolved in 0.85 p. c. solution of sodium chloride, and for the injections a solution was employed which corresponded to a content of 0.62 to 0.7 p. c. of copper. The injections caused inflammatory swellings and sometimes necroses. Out of twelve cases the tumour disappeared completely in three cases, in two cases the tumour diminished in size, in five cases the process was arrested, and in two cases the tumour grew larger.

Coryfin.

In the treatment of affections of the nose and pharynx H. Daac prefers the use of coryfin* in the form of inhalations,

Gelarie, British Medical Journal 1913, II, p. 222.

Daac, Allgemeine medizinische Zentralzeitung 1913, No. 26, p. 312.

* Compare Merck's Reports 1906—1912.

and speaks highly of its action. It proved especially useful in cases of chronic pharyngitis, and in patients who have to do much speaking such as orators, teachers and singers, who suffer from the distressing symptoms of chronic pharyngitis. The author found that these symptoms disappeared under coryfin treatment and the voice regained its former power and clearness. The mucous membranes become paler, thus affording objective proof of the action of the preparation.

J. Rossijsky, too, employed coryfin with successful results in the treatment of affections of the nasal mucous membrane and of the pharynx. He found that painting the nasal mucous membrane with coryfin rapidly alleviated the feeling of discomfort by reducing the swelling and checking the catarrhal secretion. The introduction of a pledget of cotton wool dipped in coryfin into the lower part of the nose is also very effective; as a rule this application should be repeated three times a day. The internal administration of coryfin in the form of bonbons is less effective than inhalation. Coryfin is also a good remedy for migraine and headaches. A pleasant sensation of coolness is produced within a short time by painting the upper part of the forehead with coryfin, and in the course of ten or fifteen minutes the headache disappears or is considerably alleviated. K. Kirchner also observed in diseases of the ear an improvement in the neuralgic affections after painting the painful places with coryfin. In acute catarrh of the middle-ear as a trial he applied the remedy into the Eustachian tube, as it is well known that the swelling of the mucous membrane of the tube, in particular of the tube mouth, is the principal cause of the catarrhal symptoms. To avoid irritation he employed a mixture of equal parts of coryfin and liquid paraffin which was at first applied daily for four or five days and then at intervals of two or three days, in the following manner: By means of a pipette the author introduced about five to ten drops of the coryfin-paraffin mixture into a suitable Eustachian catheter and pressed the mixture into the Eustachian tube by a strong current of air. The result was good in every case; after a short time the stuffy, blocked-up feeling of the ear and the giddiness dis-

Rossijsky, *Therapeutisches Obshrenie* 1913, No. 5.

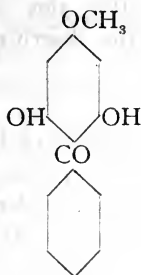
Kirchner, *Münchener medizinische Wochenschrift* 1913, No. 35, p. 1934.

appeared. Symptoms of irritation did not occur. Kirchner also succeeded in relieving the irritation in the external auditory canal by painting with coryfin.

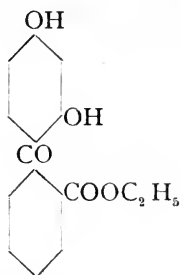
Cotoin and Resaldol.

Cotoin (genuine) is the active principle of genuine Coto bark, the origin of which is unknown. Chemically it is methyltrioxybenzophenone having the formula given below. It occurs as a yellow crystalline powder, soluble in alcohol, ether and chloroform; it is only very slightly soluble in water. Melting point 130° — 131° C.*.

Resaldol is resorcin benzoyl carbonic acid ethyl ester (2,4-dioxybenzoyl-o-benzoic acid ethyl ester), a pale yellow, crystalline substance, very sparingly soluble in water. Melting point 134° — 136° C.



Cotoin



Resaldol

The pharmacological investigation of both substances was undertaken by E. Impens. Cotoin is used as an anti-diarrhoeic in doses of 0.1 to 0.2 gramme ($1\frac{1}{2}$ —3 grains), but the property of the drug to which this action is due has not yet been conclusively established. It is devoid of anti-septic and astringent properties, but, according to Albertoni, it displays a vaso-dilator action in the splanchnic region. Impens states that the antidiarrhoeic effect of the drug cannot be ascribed to this action, since there exist a number of remedies which cause dilatation of the intestinal vessels and yet have no action in diarrhoea. On the other hand, in experiments on animals the author found that cotoin exerts a powerful influence on the tone and pendular movements of

* Compare Merck's Report 1903, p. 55.

Impens, Deutsche medizinische Wochenschrift 1913, No. 38, p. 1827.

the intestinal musculature, therefore its action consists in diminishing the tone and peristaltic action.

Resaldol acts similarly, and can therefore be used in therapeutics as an antidiarrhœic in the same manner as cotoin. According to Impens, in contrast to cotoin resaldol has the advantage of being tasteless and non-irritant, and is free from secondary effects due to its absorption. It is very slowly absorbed, whereby its local action is enhanced. It is advisable, before administering the drug, to cleanse the bowels by giving a purgative such as calomel or castor oil. The dose is 0.5 gramme ($7\frac{1}{2}$ grains) three times a day; children are given correspondingly smaller doses, according to age. The drug is given in a little water or gruel*.

L. Weil has treated 23 cases of various forms of enteritis with resaldol and obtained in almost every case an improvement or complete recovery after one or two days. In his experience it is also useful in the diarrhœa of phthisis.

Crotalin.

Further reports on the use of the venom of the rattlesnake (*Crotalus adamanteus*), introduced by Th. J. Mays and R. H. Spangler for the treatment of respiratory affections and in particular of epilepsy, have been published by Spangler, Fackenheim, Mays and A. Erlenmeyer.

According to the statements of these authors crotalin contains two albumin-like bodies, one of which has a neuromuscular and the other a hæmolytic action. The therapeutic value of rattlesnake venom is assumed to be due to this hæmolytic action, or rather to the property of crotalin of inhibiting coagulation.

* Compare Apotheker-Zeitung 1913, No. 74, p. 733.

Weil, Deutsche medizinische Wochenschrift 1913, No. 46, p. 2243.
Mays, Boston Medical and Surgical Journal 1909, Vol. 160, No. 15, p. 481 (15th April). — American Journal of Clinical Medicine 1909, December.

Spangler, New York Medical Journal 1910, September 3 and 1911, September 9; Merck's Report 1911, p. 206.

Spangler, New York Medical Journal 1913, Vol. 97, No. 14, p. 699.

Fackenheim, Vortrag auf der 6. Jahresversammlung der Gesellschaft deutscher Nervenärzte in Hamburg, September 1912. — Zentralblatt für die gesamte innere Medizin und ihre Grenzgebiete 1913, Vol. 4, p. 415.

Mays, Medical Record, March 29, 1913.

Erlenmeyer, Berliner klinische Wochenschrift 1913, No. 18, p. 817.

gulability of the blood. For instance, Fackenheim was able to demonstrate that crotalin is capable of inhibiting the tendency of the blood to coagulate. Since it has been experimentally established that the blood of epileptics shows increased coagulability, and also that coagulation takes place quicker shortly before an attack than after a fit, the aim of treatment with crotalin is to inhibit the coagulability of the blood and through this alteration in the blood to exert a beneficial influence on the epileptic fits. To this is added the sedative effect of the other above mentioned albuminous substance (according to Spangler a peptone) on the nervous system.

With crotalin treatment it is necessary to individualize. Therefore, small doses are given at first in order to establish the patient's tolerance, and the subcutaneous, or intramuscular, injection is repeated only after the disappearance of local reaction at the site of injection. Hence the repetition of the injection is regulated according to the character of the fits and the severity of the local reaction. According to Erlenmeyer the smallest initial dose is 0.000325 gramme ($\frac{1}{200}$ grain). As soon as the inflammatory reaction which always occurs at the site of injection, but which becomes less marked with each subsequent injection, subsides, after eight days a second injection of 0.00065 gramme ($\frac{1}{100}$ grain) is given. This injection is repeated at intervals of eight days, in all about four to six times. The dose is then increased to 0.00086 gramme ($\frac{1}{80}$ grain) of which two injections, at intervals of a fortnight, usually suffice. After a further interval of a fortnight a dose of 0.0013 gramme ($\frac{1}{50}$ grain) is given and this injection is repeated after four weeks. If epileptic attacks still occur, after four weeks the dose is increased to 0.0025 gramme ($\frac{1}{25}$ grain) of crotalin, and the same dose may be repeated four weeks later. If the fits remain absent an increase in dosage is unnecessary. In children and young persons the two smallest doses mentioned above should not be exceeded and the injections should be given at intervals of ten days.

May also tried crotalin in pulmonary tuberculosis and records satisfactory results, not only in the initial but also in advanced stages. For subcutaneous injection he used a solution of 0.06 gramme (1 grain) of crotalin in 24 c. c. (400 min.) of water and 6 c. c. (100 min.) of glycerin, of which 0.3 c. c. (5 min.) is equivalent to 0.0006 gramme ($\frac{1}{100}$ grain) of crotalin. The solution was injected into

the upper arm, or into the cervical region, between the lower jaw and the clavicle. The author gave as a dose 0.0003 to 0.0012 gramme ($\frac{1}{200}$ — $\frac{1}{50}$ grain), but considers 0.0006 gramme ($\frac{1}{100}$ grain) the maximum dose for injections into the neck. Later Mays administered croctalin in the form of intrapulmonary injections, especially into the caverns, beginning with a dose of 0.00008 gramme ($\frac{1}{800}$ grain) and increasing up to 0.0003 gramme ($\frac{1}{200}$ grain), given at intervals of five or six days. However, the inhalation of the remedy every three or four hours in the form of a spray and in daily doses of 0.0006—0.0012 gramme ($\frac{1}{100}$ — $\frac{1}{50}$ grain) proved most effective. On the other hand, the intravenous exhibition of the remedy is not to be recommended, as it offers no advantages and possesses several drawbacks*. Mays expects the best results from the simultaneous use of the remedy in the form of subcutaneous injections and inhalations. So far he found that the use of croctalin displays a beneficial effect on cough, hoarseness, expectoration, hæmoptysis, pains, fever, night-sweats, appetite, general health and local processes.

Cusylol.

The name of cusylol is applied to a citrate of copper** prepared according to von Arlt's directions; it is issued in three forms.

1. Cusylol (Cupri citras solubile Arlt) is a crystalline blue powder, soluble in water; it is used only for the preparation of eye-washes. Its solutions are not stable, therefore, according to B. Tristaino, should always be freshly prepared, or, according to von Arlt kept in bottles coated with paraffin. For the treatment of old and recent cases of trachoma with slight discharge, and follicular conjunctivitis, at first a 2 p. c. solution of cusylol is instilled copiously three to five times daily, so that it remains as long as possible in contact with the conjunctiva. In catarrhal conjunctivitis, in particular in cases occurring after blepharadenitis, von Arlt states that solu-

* Compare E. Harnack and H. Hildebrandt, *Experimentelle Beobachtungen über die Vergiftung mit Klapperschlangengift*, *Münchener medizinische Wochenschrift* 1912, No. 26, p. 1426.

** Compare Merck's Reports 1902, p. 47; 1903, p. 57; 1904, p. 52. von Arlt, *Wochenschrift für Therapie und Hygiene des Auges* 1913, No. 37, p. 301.

Tristaino, *Archivio di ottalmologia*, Vol. 19, No. 8, p. 527.

tions of zinc sulphate may be advantageously replaced by the following stable solution:

Cusylol	0.5 gramme	(7½ grains)
Acid. boric.	3.0 grammes	(45 grains)
Aq. dest.	100.0	„ (3⅓ oz)

M. Filtra. Sig.: 2 to 3 drops to be instilled several times daily.

2. *Pulvis Cusyloli ad unguentum*, which is used for preparing ointments with glycerin of starch or any other hydrophilic ointment base, such as resorbin ointment (Agfa). In old cicatricial trachoma and in cases of trachoma with slight discharge a two to five per cent. ointment is used, which is applied every evening by the patient. The ointment may also be used for after-treatment.

3. *Pulvis Cusyloli ad inspersionem* is uniformly brushed over the conjunctiva of the everted lids. After closing the lids a pale green thread forms in the conjunctival sac and is removed after an hour or two by means of a pledget of cotton wool dipped in water. *Pulvis cusyloli ad inspersionem* is the most effective preparation of cusylol. It is employed in all recent affections of the conjunctiva, at least at the commencement of treatment, in acute and subacute forms, during the stage of secretion until it is stopped. The other two preparations may also be used at the same time. While the application of cusylol ointments and eye-washes may be entrusted to the patient the dusting powder must always be applied by the doctor himself. The more severe the inflammatory symptoms are, the more often and more freely should the powder be applied. It acts without causing pain or irritation and offers a complete substitute for silver nitrate and copper sulphate points.

Cycloform.

The use of cycloform* in ulcers of the leg is discussed by M. Käsbohrer, F. Franke and Saar.

According to Käsbohrer, cycloform is especially useful as an anæsthetic in the treatment of varicose ulcers because it

* Compare Merck's Report 1910, p. 153.

Käsbohrer, Dissertation Munich 1912.

Franke, Ärztliche Rundschau 1913, No. 11.

Saar, Allgemeine medizinische Zentralzeitung 1912, No. 50.

displays a prolonged action without producing any symptoms of irritation. On changing the dressings every two or three days the drug is applied either in powder form or as a 5 to 10 p.c. ointment. This procedure ensures anæsthesia lasting until the following change of dressings, and in addition has a favourable influence on the granulation, epithelization and discharge. Cycloform also gives good results in burns of the first and second degree, and in tuberculous, carcinomatous and syphilitic ulcers.

Franke at first employed cycloform as a dusting powder in the treatment of painful ulcers of the leg, but later he made use of mixtures as he occasionally found that the application of the drug per se caused a slight sensation of burning. As a vehicle he employed kaolin in the following combination:

Cycloform 10.0—20.0 grammes ($\frac{1}{3}$ — $\frac{2}{3}$ oz)

Kaolin. ad 100.0 „ ($3\frac{1}{3}$ oz)

M. Tere exact. Ft. pulv. Sig.: 10—20 p.c. cycloform-kaolin powder.

The author found that in this dilution cycloform still displays an efficient anæsthetic action, and the kaolin favours the healing process. In preparing a cycloform ointment Franke emphasises the necessity of first dissolving the cycloform in oil, in order to avoid the possibility of scabbing. He advises the following formula:

Cycloform pulv. subt. 5.0 grammes (75 grains)

Solve leni calore in

Ol. oliv. 10.0 „ (180 min.)

Paraffin. dur. 3.0 „ (45 grains)

Lanolin. anhydr. ad 50.0 „ ($1\frac{2}{3}$ oz)

M. Ft. ung.

Saar states that it is quite sufficient to simply apply cycloform per se or a mixture of equal parts of cycloform and starch and then spread over the powder a little lanoline or eucerin. In contradistinction to other authors Saar was unable to observe any special influence on the healing process, but he is of opinion that granulation and epithelization might be stimulated by the simultaneous use of reliable antiseptics. The patient's greatest wish — to be freed of his pain — is fulfilled by cycloform. Of course, the use of cycloform does not do away with the necessity of applying a proper dressing.

Cymarín.

The fact that numerous authors speak favourably of the action of extract of Canadian hemp on the heart points to the presence in the extract, or rather in the drug employed in its preparation, viz., the root of *Apocynum Cannabinum*, of a substance with a digitalis-like action*. A few glucoside-like bodies have been isolated from the drug; however, they exhibited only a slight action on the heart, or none at all. As is apparent from publications which have appeared during the past year it has now been possible to obtain from the drug a chemically well defined substance. The pharmacological investigation of this body by E. Impens has shown that it displays an action on the heart similar to that of the substances of the digitalin group, and therefore is capable of therapeutic application as a cardiac tonic and diuretic. At first the term "new apocynamarin"*** was applied to this substance, but now it is placed on the market under the name of "cymarín". It is a colourless crystalline substance, with a bitter taste; it is soluble in the generally employed organic solvents and also in hot water. It is sparingly soluble in cold water. Melting point about 140° C. When treated with hot dilute acetic acid it is converted into apocynamarin***.

The clinical trial of cymarín was undertaken by M. E. Schubert, E. Allard and R. Kolb. Schubert found that in suitable doses the preparation acted on the heart and also on the kidneys. Although digitalis has a more powerful action, cymarín has the advantage that it is usually better tolerated, its dosage is more exact and consequently its action can be better controlled. Although the new preparation is not likely to supersede the use of digitalis, yet the latter may be advantageously substituted by cymarín in certain cases, in particular in chronic heart diseases. Cases may occur, as reported by Schubert and Allard, in which cymarín still displays a manifest action when digitalis and caffeine have failed. Further,

* Compare Merck's Report 1911, p. 81.

Impens, Pflügers Archiv für die gesamte Physiologie 1913, Vol. 153, p. 239.

** Compare Apotheker-Zeitung 1913, No. 28, p. 250.

*** Compare Merck's Report 1911, p. 82.

Schubert, Deutsche medizinische Wochenschrift 1913, No. 12, p. 540.

Allard, *ibid.* 1913, No. 17, p. 782.

Kolb, *ibid.* 1913, No. 40, p. 1937.

Allard points out that the diuretic action of cymarin renders the use of diuretics superfluous in the treatment of cardiac congestion. A further advantage of cymarin is to be found in the fact that the toxic and therapeutically active doses lie so far apart that its use in appropriate doses is free from danger. Kolb reports a case of chronic myocarditis with symptoms of decompensation in which an injection of cymarin yielded very good results, after digitalis, camphor, caffeine, strophanthin, venesection and amyl nitrite had in time become ineffective. He therefore feels justified in recommending the use of intravenous injections of cymarin as a life-saving procedure, or at least as being capable of prolonging life in similar cases of severe cardiac insufficiency.

Cymarin may be given per os, intravenously or rectally; subcutaneous injection is not advisable since it causes severe pain at the site of injection. Allard gives the following hints as to dosage. For internal administration very small doses should be given, i. e., 0.3 milligramme ($\frac{1}{200}$ grain) and it should not be given on an empty stomach in view of possible gastric disturbances. The author observed that vomiting and nausea occurred far less frequently with small single doses than when a dose of 0.5 to 1 milligramme ($\frac{1}{125}$ — $\frac{1}{64}$ grain) was given. The daily dose is increased to 1 or 2 milligrammes ($\frac{1}{64}$ — $\frac{1}{32}$ grain) according to the circumstances of the case and the onset of the drug's action, or of gastric or intestinal disturbances. If this daily dose fails to produce any effect it is almost useless to increase the dose and a trial may be made with the intravenous exhibition of the remedy. The above mentioned daily doses may be continued for a few days, if necessary, but after five days it is advisable to suspend administration, as the action has by now gone beyond its greatest intensity and becomes considerably weaker.

For intravenous injection the initial dose is 0.5 milligramme ($\frac{1}{125}$ grain) and Allard found that this amount is always well borne while smaller doses are uncertain or ineffective. It is true that a dose of 0.5 milligramme ($\frac{1}{125}$ grain) does not always produce a lasting effect; however, the action is usually prompt and comparatively energetic, or at least very marked. The absolutely effective dose for intravenous injection is 1 milligramme ($\frac{1}{64}$ grain). It is not advisable to exceed this dose, even should the case prove refractory to this amount. Further, the injection of 1 milligramme ($\frac{1}{64}$ grain) should

be given on the same day only in severe cases accompanied by acute troubles and when a preliminary trial dose of 0.5 milligramme ($\frac{1}{125}$ grain) has prove ineffective. Moreover, the author ceased to administer as much as 2 milligrammes ($\frac{1}{32}$ grain) as a daily dose. Usually a daily dose of 1 milligramme ($\frac{1}{64}$ grain) is sufficient and is certainly free from any injurious action. Six days was the longest period during which Allard gave the injections without an interval. For rectal use suppositories containing 0.5 to 1 milligramme ($\frac{1}{125}$ — $\frac{1}{64}$ grain) of cymarin are prescribed.

Dichlorobenzol.

Of the three isomeric dichlorobenzols, para-dichlorobenzol has recently gained importance as a moth destroyer. It forms colourless crystals, of the formula $C_6H_4Cl_2$ (1:4); melting point $53^\circ C$. It is readily soluble in alcohol, ether, chloroform, benzol and carbon tetrachloride.

The special advantages claimed for this substance as a moth destroyer are that it is an effective insecticide and when properly used innocuous to man and also to domestic animals. It has only a slight ethereal odour, which can easily be removed by airing the articles treated with the preparation. It is used in the same way as campher, employing 100 grammes of dichlorobenzol for every cubic metre of space. Besides acting as a moth destroyer, it may also be used for killing various kinds of insects, such as beetles and butterflies, and for this purpose may prove a useful substitute for potassium cyanide*.

Digitalis Substances.**

Digitalis Leaves.

Two theories are usually offered in explanation of the emetic action of digitalis, the one that the digitalis substances exert a local irritant action on the gastric mucous membrane, and the other that they display a central irritant action. To elucidate this point R. A. Hatcher and C. Eggleston gave intravenous injections of digitalis preparations to dogs

* Compare Vierteljahresschrift für praktische Pharmazie 1913, p. 125.

** Compare Merck's Report 1911, p. 31—58, and 1912, p. 159 to 167. Hatcher-Eggleston, Journal of Pharmacology and Experimental Therapy 1912, Vol. 4, p. 113.

whose intestines had been removed by operation. In the great majority of cases the movements occurring in the act of vomiting and nausea were produced in the experimental animals, thereby proving the existence of a central vomiting effect. The authors came to the same conclusion when studying the effects of digitalis substances given by mouth, for they found that especially those substances which are rapidly absorbed by the digestive apparatus displayed a far more frequent and more powerful emetic effect than substances which are absorbed with difficulty.

Josué and Godlewski attempted to solve the question whether the digitalis substances are really capable of raising the blood pressure, as is generally accepted, and whether in this case the use of digitalis is contra-indicated in the presence of high blood pressure. They employed digitalin Nativelle* for their experiments on 47 persons, and they found that the blood pressure was not altered even by large doses and on prolonged administration of the drug. Only in marked cardiac weakness did they note an increase in pressure. Based on these results the authors feel justified in stating that digitalis has no influence on the blood pressure.

Further reports on the mode of action of digitalis, and of its glucosides, which to a great extent have only special interest and cannot be briefly discussed, have been published by E. Romberg, R. Kauffmann, W. Straub, V. Weizsäcker, A. Holste, A. R. Cushney, E. Bernoulli, R. A. Hatcher and Oppenheimer. For methods of

Josué-Godlewski, Société médicale des hôpitaux de Paris 1912, November. — Deutsche medizinische Wochenschrift 1913, No. 5, p. 248.

* Compare Merck's Report 1911, p. 40.

Romberg, Münchener medizinische Wochenschrift 1913, No. 1, p. 1.
Kauffmann, Zeitschrift für experimentelle Pathologie und Therapie 1913, Vol. 12, p. 165.

Straub, Archiv für experimentelle Pathologie 1913, Vol. 71, p. 139.

Weizsäcker, *ibid.* 1913, Vol. 72, p. 347.

Holste, *ibid.* 1912, Vol. 70, p. 435.

Cushney, Berliner klinische Wochenschrift 1913, No. 16, p. 717.

Bernoulli, Münchener medizinische Wochenschrift 1913, No. 18, p. 967.

Hatcher, Journal of the American Medical Association 1913, p. 386.

Oppenheimer, Biochemische Zeitschrift 1913, Vol. 55, p. 134.

standardising digitalis reference should be made to the publications by Focke, F. Flury and W. H. Martindale.

Oigaard and H. Strauss report on the administration of digitalis leaves. Oigaard suggests that on opening an original bottle of standardised digitalis leaves in powder the contents should be divided into doses of 0.125 gramme and put up in small glass tubes closed with a cork and paraffined. In this way the digitalis powder is protected from subsequent injurious influences and retains its potency for months or even for years. The patient is instructed to open one of these glass tubes once daily after dinner and to pour the contents into an empty cup which is then filled with boiling water and allowed to stand for about ten minutes, stirring frequently. This infusion is drunk together with the powdered leaves. By this means the patient obtains an always freshly prepared infusion of digitalis of uniform activity, which is so diluted that in most instances it is well borne. This treatment can be repeated for five days in succession, whereupon an interval of two days should be allowed. In severe cases the above mentioned dose may be given twice.

In hydropericarditis and hydronephrosis Strauss recommends a combination of cardiac tonics with diuretics, as by this means not only the added effects of both are produced, but an action can be obtained which is far superior to that of the former. On the basis of his clinical experience he advocates the following combinations, with which he has obtained good results.

Rp. Infus. Fol. Digital. titr. 1 gramme (15 grains) et Scill. 5:150 (75 grains : 5 oz), Diuretin. 10 grammes (150 grains), Tinct. Strophanth. 3 grammes (50 min.), Spartein. sulph. 0.1 gramme ($1\frac{1}{2}$ grains), Syr. Juniper. ad 180 grammes (6 oz). M. Sig.: 1 tablespoonful four times a day.

Rp. Infus. Fol. Digital. titr. 1 gramme (15 grains) Scill. 5:150 (75 grains : 5 oz), Euphyllin. 2.5 grammes (40 grains), Tinct. Strophanth. 2.5 grammes (40 min.), Spartein. sulph. 0.1 gramme ($1\frac{1}{2}$ grains), Tinct. Opii 1 gramme (17 min.), Mucil.

Focke, Zeitschrift für experimentelle Pathologie 1913, Vol. 14, p. 262.

Flury, Pharmazeutische Praxis 1913, No. 1.

Martindale, Pharmaceutical Journal 1912, Vol. 35, p. 745.

Oigaard, Ugeskrift for Laeger 1912, No. 44.

Strauss, Therapeutische Monatshefte 1913, No. 3.

acac. ad 180 grammes (6 oz). M. Sig.: two tablespoonfuls twice daily as an enema.

Adigan.

Adigan, according to S. Fränkel and P. Kirschbaum, is a preparation of digitalis which has been freed from the emetic substances having an irritant effect on the stomach. Using the fact that the saponin bodies display an irritant action on the gastro-intestinal tract as a basis, the authors attempted to remove these from digitalis extract by the digitonin-cholesterin method of precipitation, which, as is known, was proposed by Windaus for the quantitative estimation of cholesterin by digitonin. They therefore treated extracts of digitalis with cholesterin and by this means obtained a preparation which should be free from the known unpleasant secondary effects of infusion of digitalis. In experiments on animals they found that this purified preparation always caused stillstand of the heart in systole, whereas not purified preparations with striking frequency caused stoppage of the heart in diastole. As yet no reports are available regarding the mode of administration, dosage and clinical results.

Cordalen.

As was stated at the time with digalen, cordalen is also said to be a solution of digitoxin, at least it is described as digitoxin verum puriss. cryst. solutum. As it is also said to be non-irritant Koebbel undertook experiments with this preparation. He found that in cardiac insufficiency a subcutaneous dose of 0.5 c.c. displayed a prompt effect, but it gave rise to pains and infiltrations which in one case persisted for weeks, in spite of the application of moist compresses and ichthyol packs. According to the author's statements cordalen cannot be described as non-irritant.

Digalen.

According to W. Sternberg, with digalen it is not only possible to regulate the heart's action in suitable cases, but it is also capable of removing the tormenting symptoms of insomnia. This is especially the case with older persons suffering

Fränkel-Kirschbaum, Wiener klinische Wochenschrift 1913, No. 16, p. 605.

Koebbel, Deutsche medizinische Wochenschrift 1913, No. 40, p. 1938.
Sternberg, Therapeutische Monatshefte 1913, No. 5, p. 358.

from arterio-sclerosis and irregularity of the cardiac functions. The author reports a case of arterio-sclerosis in which all other hypnotics had failed, whereas digalen displayed a prompt hypnotic action. E. Steiner and F. Laube report two cases of cardiac weakness in which the intravenous injection of digalen* yielded excellent results.

Digifolin.

Owing to its freedom from irritant action digifolin is also intended to meet the demand for an active preparation of digitalis capable of subcutaneous exhibition. According to C. Hartung, it is free from saponins and potassium salts, and contains all the active principles of digitalis in their natural proportions. For internal administration it is issued in tablets, and for subcutaneous injection in ampoules**.

E. F. Zurhelle states that treatment by the subcutaneous exhibition of digitalis is made possible by digifolin, as this preparation only causes redness and swelling at the site of injection, which is slightly sensitive to touch. Only in rare cases did the patients complain of real pains, particularly if the injections were made too superficially, i. e., intracutaneously. Subcutaneous injection is especially indicated in chronic hepatic forms of cardiac insufficiency. In these cases 0.3 to 0.4 gramme of digitalis should be given daily for three or four days in order to obtain a full digitalis action which is then maintained by doses of 0.1 to 0.2 gramme of digitalis. This dose should not be exceeded in the presence of renal complications***. In acute insufficiency the author prefers subcutaneous to intravenous injection, and in urgent cases recourse should be had to measures with a prompt action, such as injections of camphor or constriction, until the action sets in. G. Cavina never observed pain after the subcutaneous injection of digifolin, if the injection were made into healthy

Steiner, Medizinische Klinik 1913, No. 3, p. 101.

Laube, Klinisch-therapeutische Wochenschrift 1913, No. 8, p. 232.

* Compare Merck's Reports 1904—1912.

Hartung, Archiv für experimentelle Pathologie 1912, Vol. 69, p. 149
and Münchener medizinische Wochenschrift 1912, No. 36, p. 1944.

** Compare Merck's Report 1912, p. 163.

Zurhelle, Therapeutische Monatshefte 1913, No. 7, p. 479.

*** 1 tablet or 1 ampoule of Digifolin is equivalent to 0.1 gramme of Folia Digitalis.

Cavina, Archivio di farmacologia sperimentale 1913, Vol. 15, p. 547.

tissue. It acted quickly if 2 to 3 c.c. were injected subcutaneously in severe cases, or four to five tablets given by mouth; otherwise two to three tablets were sufficient, and for permanent treatment half to one tablet daily. With this medication the author obtained a prompt action on the pulse and secretion of urine in chronic endocarditis and myocarditis.

E. Löwenheim was also satisfied with the effect of digifolin in secondary cardiac weakness, mitral defects, affections of the cardiac muscle and cardiac weakness associated with congestion. Usually he administered it per os, giving one tablet (= 0.1 gramme of digitalis leaves) five times a day. After three days he allowed an interval of at least eight days.

Digipan is the name of a new preparation of digitalis which contains the active principles of digitalis but is free from digitonin. It occurs as a white amorphous powder, soluble in all proportions in alcohol and chloroform, and soluble 1 in 700 of isotonic nutrient saline solution. It is issued in liquid form (1 c.c. = 24 drops = 0.1 gramme of digitalis leaves), and in tablets (1 tablet = 0.05 gramme of digitalis leaves). According to K. Weiss it is a useful preparation of digitalis. He administered it by mouth in doses of one tablet three times a day, or fifteen drops two to three times daily, or 1 c.c. intramuscularly or intravenously, in obstinate cases 1 c.c. twice a day. He does not advocate subcutaneous injection as it causes disturbances.

Digipuratum.

Digipuratum, which has been repeatedly discussed in my Annual Reports*, is now supplied in three forms. For internal use it is issued in tablets, each tablet corresponding to 0.1 gramme of digitalis leaves, and in alcoholic solution, of which four drops exhibit the same activity as 0.01 gramme of digitalis leaves. The sterile digipuratum supplied in ampoules is intended for intramuscular and intravenous use; one ampoule = 0.1 gramme of digitalis leaves.

Löwenheim, Münchener medizinische Wochenschrift 1913, No. 45, p. 2502.

Weiss, Münchener medizinische Wochenschrift 1913, No. 45, p. 2499.

* Compare Merck's Reports 1909—1912.

Further reports on the therapeutic value of this preparation have been published during the past year by R. Joseph, Ph. Baumann, E. Keuper and G. Malan.

Joseph undertook to solve the question whether it were possible to produce not only an action on the heart but also on the vessels by the intravenous injection of therapeutic, non-toxic, i. e., small doses of digitalis. For his experiments he used digipuratum and g-strophanthin. The experiments were made on rabbits which were injected with the digitalis preparation during urethane anæsthesia. His investigations showed that after the administration of both substances in doses still capable of displaying an action on the heart an effect on the vessels was also plainly manifest. The latter usually led to a slowly developing and lasting constriction of the intestinal vessels.

Baumann has used digipuratum in myocarditis associated with arrhythmia, especially in elderly patients, in valvular defects associated with œdema, and also in pneumonia, dyspnoea and similar indications for digitalis treatment. He gave one tablet per os three times a day and always obtained a satisfactory result, even in cases where digalen, infusion of digitalis, etc., had failed or had lost their action. Malan, who administered the preparation internally and intravenously, extols not only its prompt action, but also the absence of unwelcome secondary effects and the reliability of the dosage. Except in the treatment of pneumonia and other infections, digipuratum, particularly when combined with diuretin, is principally indicated in valvular defects. Keuper prescribed liquid digipuratum which proved itself a potent substitute for infusion of digitalis in all cases where digitalis is indicated. With one sole exception no irritant action on the gastric mucous membrane was observed. According to this author's experience the preparation may also be injected subcutaneously. In only two cases did this method of application cause small painful infiltrations which soon disappeared. This treatment proved particularly effective in cardiac weakness, mitral defects, arterio-sclerosis and myocarditis asso-

Joseph, Archiv für experimentelle Pathologie 1913, Vol. 73, p. 81.

Baumann, Allgemeine medizinische Zentralzeitung 1913, No. 3, p. 27.

Keuper, Therapeutische Monatshefte 1913, No. 9, p. 641 and No. 10, p. 756.

Malan, Medicina Nuova 1913, No. 16. — Petersburger medizinische Wochenschrift 1913, No. 15, p. 186.

ciated with failing compensation, if immediately at the beginning of treatment 1 to 2 c. c. of digipuratum were injected intravenously, continuing the treatment by giving 0.1 gramme of digipuratum by mouth three times a day. In every case the author succeeded in producing copious diuresis within two to three days by this method.

Digitonin, Crystalline

To distinguish animal oils from vegetable oils J. Marcusson and H. Schilling have elaborated a method which is based upon Bömer's phytosterin acetate test and Windaus' method of determining cholesterol by means of digitonin*. It is well known that the animal fats contain cholesterol and the vegetable fats phytosterin, alcohols which are easily distinguishable by the forms of their crystals and the melting points of their acetic acid esters. Their extraction from the saponified fats and purification according to Bömer's method is, however, costly and tedious, wherefore the above named authors effect their separation by the method proposed by Windaus of precipitating with digitonin. This procedure is all the more simple since it can be carried out directly with the fatty oil without previous saponification and extraction of the phytosterin and cholesterol.

50 grammes of the warmed oil or fat to be analysed are well shaken with 20 c. c. of a 1 p. c. alcoholic (96 p. c.) solution of digitonin for fifteen minutes in a separator, and after standing for several hours the oily layer which has separated is drawn off. The flocculent precipitate of digitonid (of the cholesterol or phytosterin) present in the alcoholic layer is shaken with 50 to 100 c. c. of ether to remove the fatty oil, and the air-dried digitonid is also purified with ether. Thereupon it is heated with 1.5 c. c. of acetic anhydride in a narrow test-tube for half an hour. The acetic acid esters (acetates) thus obtained are crystallised from alcohol once or twice and their melting points determined. Cholesterol acetate melts at 114.3°—114.8° C., and phytosterin acetate at 125.6°—137° C. In the case of vegetable oils the acetate obtained, as the authors have experimentally established, melts at about 124°—135° C., and with animal oils at 111° to 114° C., according to the oil employed**, whereas mixtures

Marcusson-Schilling, *Chemiker-Zeitung* 1913, No. 100, p. 1001.

* Compare Merck's Report 1911, p. 74.

** Compare the table in the original work.

of animal and vegetable oils yield substances with a melting point above 116° C. Therefore, if the acetate has a melting point below 116° C. this is evidence of a pure animal oil; if it melts at 116° C. there is a suspicion of the admixture of vegetable oil; and if it melts above 116° C. this is proof of the admixture of vegetable fat. The authors found, for instance, that a mixture of 90 parts of neatsfoot oil and 5 parts of rape oil yielded an acetate which after twice recrystallizing melted at 117° — 119° C. A content of 10 p. c. of rape oil yielded an acetate melting at 119° C.*

M. Klostermann thinks it advisable to first saponify the fats, as digitonin only precipitates the free sterins and not their esters. His method is as follows:

A solution of potassium hydroxide is prepared by dissolving 200 grammes of potassium hydroxide in 200 c. c. of water and then adding 700 c. c. of alcohol (94 p. c.). 100 grammes of fat are saponified on the water-bath with 200 c. c. of this solution of potassium hydroxide, which is accomplished in a few minutes, and the cooled, clear soap solution is diluted with 300 c. c. of water. Thereupon 100 c. c. of hydrochloric acid (25 p. c.) are added and the mixture is shaken with 250 c. c. of ether in a separator. The ethereal solution thus obtained of the fatty acids, after drawing off the aqueous layer, is twice shaken with 50 c. c. of water, 250 c. c. of petroleum ether are added, and then 25 grammes of sodium chloride (to clarify). It is now filtered through cotton wool into a flask with a capacity of 500 c. c. and while warm mixed with a solution of 1 gramme of digitonin in 20 c. c. of alcohol (90 p. c.). After about a quarter of an hour the digitonids which have separated are collected and well washed with ether. This is followed by acetylation, purification of the acetyl sterins and recrystallisation from alcohol.

Dinitrophenol Sodium.

A technical dinitrophenol sodium in paste form is issued under the name of "mykantin". According to Falck, this

* For the quantitative estimation of cholesterin in blood, etc., compare the article on Cholesterin in this Report.

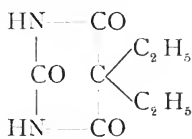
Klostermann, *Zeitschrift für Untersuchung der Nahrungs- und Genußmittel* 1913, Vol. 26, p. 433.

Falck, *Pharmazeutische Zeitung* 1913, No. 52, p. 512 and No. 75, p. 751.

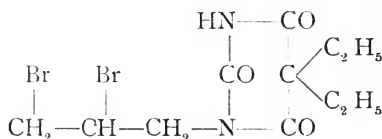
preparation, which is readily soluble in water, has proved very effective against dry rot. A 1 in 250,000 dilution still prevents sporulation and the development of spores of wood-destroying fungi, without attacking wood or iron parts. In addition it colours the wood so treated, thus enabling a control of the disinfection. By the addition of suitable substances dinitrophenol sodium is deprived of its explosive properties. For practical purposes it is sufficient to paint the wood with, or dip it into, a 2 to 4 p. c. solution of dinitrophenol sodium in water in order to impart to the wood a sufficient degree of protection. This protection is also permanent, as the spores of the fungi come from the outside and must penetrate along the same passages as the disinfecting solution. On the other hand, it is important to carry out the disinfection of the wood at the earliest possible moment, before it has been more or less destroyed. For this reason it is advisable to apply the preparation to the cross-cut surfaces of the wood immediately after felling the trees, since the spores of the fungi here find an easy entrance. The disinfection of timber for building purposes is best done in the timber yard, and all cut sections made in the course of building should also be treated.

Diogenal.

Diogenal, a derivative of veronal, is dibromopropyl-diethyl-barbituric acid:



Veronal



Diogenal

Diogenal occurs as a fine, white crystalline powder with a faintly bitter taste. It is almost insoluble in water, and is not acted upon by acids, such as the acids of the gastric juice. In the alkaline intestinal juice it is dissolved. In addition to being soluble in alkalies it dissolves in alcohol, ether and fats. Melting point 125° C. Diogenal contains 41.6 p. c. of bromine.

Although veronal, according to R. Heinz, when administered in rational doses may be regarded as absolutely non-

toxic, there is some justification for seeking for a "milder acting veronal" among the derivatives of veronal, or for combining veronal with chemical bodies or chemical groups displaying an analogous action with a view to ascertaining whether a different or more comprehensive effect may be obtained by this means. For this reason Heinz undertook the pharmacological investigation of diogenal, and his results may be summarized as follows:

Experiments on animals showed that diogenal is at least four times less toxic than veronal; however, the action displayed by diogenal is also less energetic, i. e., diogenal has a milder action. This property of the new preparation not only permits its use as a hypnotic, but also as a general sedative. The repeated administration of average and large doses did not cause any functional or organic disturbances, nor any deleterious effect on the blood. With regard to any influence on the heart and circulation, no change in the pulse or blood pressure after the administration of diogenal was demonstrable in animal experiments.

The bromine present in diogenal is excreted very gradually, and is in large part retained within the organism. Therefore, it is well able to display its effect in sick persons, all the more as the bromine contained in diogenal is split off in the organism, and in the form of bromine ions is able to display its therapeutic activity. Of special importance in this connexion is the fact that with the administration of diogenal the amount of bromine stored up in the body is increased.

The results of its pharmacological study, according to Heinz, point to the following conclusions regarding its therapeutic employment: "Compared with veronal it has the advantage of being considerably less toxic, and this was proved by the absence of any after-effects or secondary action whatever when administered to man, even after its prolonged use. The hypnotic dose of diogenal is three to four times larger than that of veronal. Moreover, the action of diogenal is milder. It is necessary for the practitioner to have a number of hypnotics at his command, since in practice, as is well known, a change in hypnotics is often indicated. Of course, recourse will first be had to as "mild" a hypnotic as possible, and diogenal is eminently suited for this purpose. One gramme (15 grains) of diogenal may be taken to represent the average sleep-inducing dose for adults; the delayed onset of action

must, however, be taken into account. The investigation of diogenal as a general sedative appears more promising. Here the mitigated, or milder, form of veronal action, combined with the action of the bromine component, should display an effect not obtainable by the use of bromine alone. The innocuousness of diogenal permits the administration of larger single doses, as well as its prolonged use. The results obtained by its administration to patients were surprisingly good and encourage a more exhaustive study of the preparation."

In confirmation of Heinz's experimental findings F. Mörchén states that diogenal as a sedative is scarcely approached by any other as regards efficiency, while displaying a powerful effect. He has found that it is readily taken by patients, and even in such large doses as 2 grammes (30 grains) [4 to 5 grammes (60—75 grains daily)] does not produce any unwelcome secondary effects; it is useful in all forms of nervous diseases and psychoses in which sedatives are indicated. The average dose in conditions of extreme excitement is 1 gramme (15 grains) three times a day, and in milder forms of restlessness 0.5 gramme ($7\frac{1}{2}$ grains) three times daily. The author never observed any cumulative action. According to Mörchén, diogenal should prove useful in epilepsy and also in "neurasthenic" conditions of restlessness and anxiety which are not really psychotic. He reports the case of a patient treated for morphine habit to whom he gave a few times 1 gramme (15 grains) of diogenal in the afternoon to relieve his discomfort, and already half an hour after its administration its good action was apparent. The restlessness and depression which always came on towards the evening remained entirely absent.

J. Bujdosó is able to confirm the results of Mörchén's investigations, although he lays greater stress upon the narcotic than upon the sedative properties of diogenal. According to this author's exhaustive investigations diogenal deserves full consideration as a hypnotic, even in cases where for any reason a change in the soporifics used is indicated. It is also very useful as a sedative. If it is administered during the day the nerves are calmed to such an extent that at night time the use of a hypnotic is rendered superfluous.

Mörchen, Münchener medizinische Wochenschrift 1913, No. 48, p. 2671.

Bujdosó, Gyogyaszat 1913, No. 38.

The author also tried diogenal in epilepsy and found that it proved as effective as the use of bromides. In one case which did not react to bromides diogenal also failed. Bujdosó gave 1 gramme (15 grains) morning and evening.

Dionin.

As J. Kayser already had occasion to report some years ago*, dionin has proved itself an indispensable drug in eye work, particularly in the treatment of various corneal affections. According to a recent communication he still employs as a rule a 2 p. c. solution which is instilled three times a day, in addition to the application of warm compresses. In his experience this treatment leads to an appreciable improvement usually after three or four days. In such cases atropine may be entirely dispensed with. In deep keratitis where involvement of the iris is apprehended, or where this has already occurred, Kayser instils three times a day, or even every two hours, dionin and atropine, and after the keratitis has healed, especially if central macula is present, he applies for some time 3 p. c. yellow mercuric oxide ointment, to which he adds every second day a little dionin in powder. The author has had an extensive experience of dionin and in agreement with other investigators he has found that it possesses a clearing up effect. He has not undertaken any special experiments to establish the analgesic action of dionin, but on using this drug he always observed that after the disappearance of the symptoms of irritation which follow its application it alleviated or removed the pain.

According to H. E. Götz, dionin deserves special consideration in the treatment of hay fever. The author has elaborated a method which he claims to be the best palliative treatment known to him. It carries the patient through the whole hay fever season with little or no inconvenience. His method consists of prophylactic and curative treatment. As a prophylactic measure before the onset of any symptoms of hay fever a solution of campho-menthol 10 p. c. in liquid paraffin is sprayed into the nose. This treatment is intended

Kayser, *Wochenschrift für Therapie und Hygiene des Auges* 1913, No. 26.

* Compare *Wochenschrift für Therapie und Hygiene des Auges* 1907, No. 32.

Götz, *Merck's Archives* 1913, No. 7.

to alleviate the severity of the attack; in any case, however, it is grateful to the engorged membrane of the nose and pharynx. When the phenomena of hay fever appear the author gives the following powder:

Rp. Dionin.	0.015	gramme ($\frac{1}{4}$ grain)
Atropin. sulph.	0.00012	„ ($\frac{1}{500}$ „)
Caffein. citr.	0.0075	„ ($\frac{1}{8}$ „)

at first every two, then every four hours, or until the nose is free and the throat is dry. As soon as the patient is under the influence of this medication he feels well and no symptoms of the affection are apparent. These do not return so long as the effect of the drugs is maintained, and the patient is able to go about his daily occupation. The lessening and disappearance of the secretions, the most inconvenient symptom of hay fever, is due to the combined action of dionin and atropine. The dionin diminishes the sensibility of the peripheral nerve-endings in the nose and thereby causes the sneezing to cease. The action of dionin is assisted by the atropine, which also checks the discharge, and by the caffeine which has a slightly stimulant action. To meet any objections Götz states that he has never observed any habituation to dionin, nor did his patients complain of constipation. Of course, this treatment is continued only during the hay fever season.

In non-syphilitic ozæna, in addition to irrigation with a lukewarm solution of hydrogen peroxide, Heil recommends the use of a snuff consisting of 0.5 gramme ($7\frac{1}{2}$ grains) of menthol, 0.1 gramme ($1\frac{1}{2}$ grains) of dionin, and 5 grammes (75 grains) of milk sugar; every night the nasal cavity should be thoroughly cleansed with 20 p. c. boric acid ointment.

Dionin is also very useful in chronic middle-ear catarrh. B. A. Randall found that the intratubal application of a 2 p. c. dionin solution at first causes injection of the structures of the middle-ear, however, in many intractable cases it then makes it possible to effect a cure.

G. Liebermeister's paper is an interesting contribution to the treatment of heart diseases. He states that in cardiac disease it is imperative to regulate not only the heart's action

Heil, *Ars Medici* 1913, No. 6.

Randall, *Monatsschrift für Ohrenheilkunde und Laryngo-Rhinologie* 1913, Vol. 47, No. 1.

Liebermeister, *Medizinische Klinik* 1913, No. 30, p. 1214.

but also to regulate the respiration and renal function, and at the same time the nervous system should be calmed. Since the functional disturbances of the several organs and the correlation of the different disturbances are not always readily recognizable, and as the most pronounced organic functional disturbances are often the most difficult to influence directly, whereas they are appreciably improved by indirect influence, the following prescription is recommended:

Rp. Dionin.	0.005—0.01 gramme	($\frac{1}{12}$ — $\frac{1}{6}$ grain)
Fol. Digital.	0.07 —0.1	„ ($\frac{1}{8}$ — $1\frac{1}{2}$ grains)
Diuretin.	0.5 —0.8	„ ($7\frac{1}{2}$ —12 grains)

M. Ft. pulv. Mitte XV in cachets.

Sig.: One cachet three times a day.

With this treatment rest in bed is necessary. As soon as the beneficial effect of the powder on the heart, respiration and diuresis becomes manifest, which often occurs within twenty-four hours, the dose is reduced to two cachets daily, and when the action is very marked only one powder is given (at night time). With due attention to individual differences, if necessary, one powder may be given daily for weeks.

F. Tomann reports on the use of dionin in veterinary practice. This author has used dionin with uniformly favourable results, especially in superficial keratitis and parenchymatous keratitis. Among other cases he treated a horse in which one eye exhibited slight hyperæmia of the conjunctiva, insignificant lacrymation and such dense corneal opacity that the eye looked like a greyish-blue spot. As deep-seated inflammation of the cornea was present, three drops of the following solution were instilled twice daily into the animal's eye:

Rp. Dionin.	0.3 gramme	(5 grains)
Atropin. sulph.	0.15	„ ($2\frac{1}{3}$ grains)
Aq. destill.	30 grammes	(1 oz)

After ten days the greyish-blue spot disappeared and the eye cleared up.

Diphenylglyoxime.

Several years ago Tschugajeff proposed the use of α -dimethylglyoxime as a test for nickel, which has since found

Tomann, Veterinärny Wratsch 1913, No. 19.

Tschugajeff, Merck's Reagenzienverzeichnis 1913, p. 360. —

Merck's Report 1905, p. 60 and 1910, p. 165.

a place in analytical chemistry for the quantitative estimation of nickel. Recently F. W. Attack has recommended α -diphenylglyoxime for the same purpose.

α -diphenylglyoxime, or α -benzildioxime, forms colourless crystals melting at 237° C.; it is almost insoluble in water, with difficulty soluble in hot alcohol, slightly more soluble in hot acetone, from which it may be recrystallized. The alcoholic solution of this substance yields with solutions of nickel salts a voluminous red precipitate, which on boiling assumes a reddish-yellow colour. It is quite insoluble in water, alcohol, acetone, 10 p. c. acetic acid, and solution of ammonia. Already at ordinary temperature the addition of a solution of nickel to a solution of diphenylglyoxime containing acetone yields a reddish-yellow precipitate.

For analytical purposes an alcoholic, or alcohol and acetone, solution containing 0.05 p. c. of diphenylglyoxime is used. According to Attack, as a test for nickel diphenylglyoxime is more sensitive than dimethylglyoxime. Tschugajeff states that in ice cooled solutions of dimethylglyoxime a red coloration is produced if nickel is present in the proportion of 1 in 400,000; according to Attack, however, the diphenylglyoxime solution mentioned above yields a reddish precipitate in the presence of the same content of nickel without cooling. He states that with his test it is still possible to demonstrate one part of nickel in five million parts of water. For the quantitative estimation of small amounts of nickel the fact would have to be taken into account that the diphenylglyoxime-nickel compound has a greater molecular weight than the dimethylglyoxime-nickel compound. For the quantitative estimation of nickel, for every 0.01 gramme of nickel 150 c. c. of a hot, saturated alcoholic solution of diphenylglyoxime are added to the nickel solution, and the mixture is heated for a few minutes on the water-bath. It is easily filtered, and the precipitate can be washed with hot alcohol and dried at 110° — 112° C.

The quantitative separation of nickel and cobalt is possible in an ammoniacal solution, as in the latter cobalt salts are not precipitated by the reagent.

Diuretin.

H. A. Christian and J. P. O. Hare undertook experiments on animals with a view to establishing to what extent the use of diuretics is contra-indicated in the presence of acute nephritis. For this purpose they produced acute nephritis in rabbits by the subcutaneous or intravenous injection of uranium nitrate, and then observed the action displayed by diuretin, which was given by mouth or by intravenous injection. The time which elapsed between the injection of uranium nitrate and the death of the experimental animal was taken as the criterion of the diuretin action. They found that in nephritis following a lethal course the administration of diuretin hastens the death of the animal. Although it does not seem admissible unreservedly to apply a conclusion drawn from animal experiments to human pathology, the authors, on the basis of the results of their experiments, feel justified in assuming that also in man diuretin might prove sometimes harmful in acute nephritis, and therefore in such cases its administration requires caution. In milder cases, however, a favourable influence may be expected from its use.

Of interest is an observation recorded by L. Stein, who states that diuretin exerts an influence on menstruation. When prescribing this remedy he made the observation that in cases in which the period otherwise came on at the normal time, it usually appeared about eight to ten days earlier. On the other hand, in cases where menstruation was delayed diuretin caused its appearance at the normal time. The author ascribes this effect to the dilator properties of diuretin, which are worthy of attention in congestion of the uterus (e. g. endometritis) with regard to the possible presence of metrorrhagia.

Elarson.

Elarson is the strontium salt of chloro-arsenobehenic acid. It is an almost colourless, amorphous powder, insoluble in water, which decomposes on heating and has no definite melting point. It contains about 6 p.c. of chlorine and about 13 p.c. of arsenic. According to E. Fischer and G. Klem-

Christian-Hare, Archives of Internal Medicine 1913, Vol. 11, No. 5.
Stein, Wiener medizinische Wochenschrift 1913, No. 31, p. 1906.
Fischer-Klemperer, Therapie der Gegenwart 1913, No. 1, p. 1.

perer, the chemical properties of the preparation justify the assumption that in the stomach chloro-arsenobehenic acid is liberated by the action of the gastric acid, and in the alkaline intestinal juice is converted into a soluble alkaline salt, in which form it is then absorbed. The clinical study of elarson by Klemperer showed that this new preparation is eminently fitted for internal arsenic medication in cases where the latter is indicated. The author gave to adults two tablets three to five days a day, to children one tablet twice or three times daily. The tablets are standardised to contain each 0.0005 gramme ($\frac{1}{125}$ grain) of arsenic, an amount which is equivalent to one drop of Fowler's solution. In secondary anæmias this dose of elarson regularly caused a considerable increase in the number of blood corpuscles; in loss of appetite and conditions of debility it led to an improvement in the general condition and to a gain in weight. It also proved useful in patients suffering from pulmonary tuberculosis, particularly during the febrile stages. According to Klemperer, it proved especially useful in chorea and in severe neuralgias, particularly in headaches which had resisted other forms of arsenic treatment. It is also worthy of attention in Graves's disease. The author never observed any unpleasant secondary effects on giving six tablets daily, and even ten tablets were almost always well borne. With the large doses only a few patients complained of gastric disturbances, and these could be obviated by giving the preparation after meals.

Elarson, according to Klemperer, represents a new form of arsenical preparation which differs from former preparations of arsenic in that it is the salt of a lipoid acid containing arsenic which is soluble in ether, and the salt which is formed in the intestines exhibits the characters of a soap. This ensures better absorption and a greater affinity for the nervous system and bone marrow.

A. Leibholz has given elarson with very good results in some cases of anæmia and chlorosis, and G. Walterhöfer in a large number of cases of secondary anæmias of various origin, such as occur, for instance, in cancer of the stomach, profuse bleeding consequent on abortion, and in excessive menstruation, or which may be caused by tubal pregnancy.

Klemperer, *ibid.* 1913, No. 4, p. 192.

Leibholz, *Therapie der Gegenwart* 1913, No. 3, p. 144.

Walterhöfer, *Medizinische Klinik* 1913, No. 42, p. 1727.

After removal of the cause of disease a satisfactory result was obtained by the use of elarson. In chlorosis, however, the results were less satisfactory. Subsequently the author left off the use of elarson in cases of chlorosis associated with marked dysmenorrhœal troubles, as in these it caused increased loss of blood. Experiments on anæmic patients with scanty menses, based on this observation, proved unsuccessful. In the treatment of pernicious anæmia, leukæmia and pseudo-leukæmia elarson does not accomplish either more or less than other preparations of arsenic, nevertheless in leukæmia and pseudo-leukæmia it permits a welcome change in arsenic medication. As secondary effects, in addition to the increased loss of blood mentioned above, the author observed diarrhœa in one case already after the administration of fourteen tablets, in another case herpes on the left breast appeared, which disappeared on stopping the use of the preparation.

A further indication for elarson is afforded by those skin diseases in which the use of arsenic is indicated, e. g., psoriasis vulgaris, verrucæ planæ et vulgares, lichen ruber planus, pemphigus vulgaris, and certain forms of eczema. G. Scherber found that the compound is as effective as other preparations of arsenic, and may be considered an efficient adjuvant to external treatment. For adults he prescribed gradually increasing doses up to three tablets three times a day, for children up to two tablets three times daily. In his experience these can be given for a prolonged period, since they cause unwelcome secondary effects only in exceptional cases.

According to G. Maier and M. Sussmann elarson is worthy of consideration in the treatment of genuine epilepsy. In the cases recorded by the authors the observation was made that under the influence of this preparation the number of the fits markedly diminished, while the mental activity showed an improvement. In the case described by Sussmann of an adult patient he gave two tablets three times a day, or 180 tablets in all.

With regard to the value of elarson in Graves's disease, O. Kohnstamm is unable to make any definite statement

Scherber, Wiener medizinische Wochenschrift 1913, No. 36.

Maier, Deutsche medizinische Wochenschrift 1913, No. 35, p. 1677.

Sussmann, *ibid.* 1913, No. 39, p. 1886.

Kohnstamm, Therapie der Gegenwart 1913, No. 11, p. 527.

as to its specific action, because in addition to special diet and physical therapy he also gave antithyroidin. He administered elarson in tablets, beginning with one tablet and increasing the dose by one tablet daily until 25 tablets were taken daily. At the same time he administered antithyroidin, beginning with one tablet and increasing the amount to 15 tablets a day. After the maximum dose of both remedies had been reached he decreased the dose of each in the same manner. The results were highly satisfactory.

Elbon.

As I have already stated, elbon is chemically cinnamoyl-p-oxyphenyl urea, a substance which is with difficulty soluble in water*. On decomposition into its components within the organism, according to A. Camphausen, it effects disinfection of the air passages in which it is deposited. In this way it alleviates the irritable cough and liquefies the expectoration, while the oxyphenyl urea set free during the process of decomposition displays an antipyretic action. Therefore, it is specially indicated in the first and second stages of pulmonary tuberculosis and their associated bronchitic affections, particularly in foetid forms. In these cases it can be given for weeks, in doses of 1 gramme (15 grains) four times a day. Based on his experience of elbon, F. Johannesohn comes to the following conclusions:

About two-thirds of the elbon given by mouth is absorbed by the body. The preparation produces an increase in the number of leucocytes and a daily increasing fall in temperature. The sputum improves both as regards quantity and number of tubercle bacilli. Cases in the initial stage with subfebrile temperatures are improved to such an extent that after a sufficiently prolonged treatment a cure can be achieved. But also in more advanced cases with cavities and a slight tendency to breaking down of tissue, which are recognizable by not too high fever, an appreciable improvement may be obtained; on the other hand, in the presence of a pronounced tendency to breaking down of tissue, i. e., cavities and high fever, it produces only a subjective and transient objective improve-

* Compare Merck's Report 1911, p. 202.

Camphausen, Zeitschrift für Tuberkulose 1912, Vol. 19, p. 327.

Johannesohn, Berliner klinische Wochenschrift 1913, No. 20, p. 914.

ment. The author states that pneumonia is also beneficially influenced by elbon.

Embarin.

This new antisyphilitic* was discussed during the past year by A. Gappisch, H. Sowade, R. von Planner, R. Fried and M. Salomonski, who report the results of their clinical investigation of this drug.

Gappisch treated twenty cases of syphilis in all stages, most of which were out-patients. The preparation is not only remarkable for its energetic action, but also for the fact that its intragluteal injection is almost entirely free from pain. In most cases of secondary and tertiary syphilis treatment may be carried out by its use alone. Sowade, too, considers embarin a good antisyphilitic which does not cause pain if the injection is properly made. He further points to the possibility of carrying out an energetic mercurial treatment in the short space of three or four weeks. In 123 clinical cases he gave for a course of treatment on an average 15 injections; at first the injections were made at intervals of five or seven days, and later every second day. The other above mentioned authors also express a favourable opinion regarding the therapeutic value of embarin; however, all are agreed that unwelcome secondary effects are by no means a rare occurrence during treatment with this drug. For instance, disturbances of the general condition and a rise in temperature were observed, and in some instances the patients complained of loss of appetite, headaches, lassitude and a feeling of weight in the limbs. Sowade does not regard these symptoms as serious, and believes that they may be ascribed to the action of large amounts of mercury. Nevertheless, if violent secondary effects occur, such as high fever, rigor and collapse, he advises breaking off the treatment. The fact that embarin is well borne locally, according to von Planner, permits its use in delicate patients, in these, however, he urges caution with regard to the doses employed, and treatment

* Compare Merck's Report 1911, p. 226.

Gappisch, *Medizinische Klinik* 1913, No. 34, p. 1377.

Sowade, *Deutsche medizinische Wochenschrift* 1913, No. 20, p. 932.

Planner, *ibid.* 1913, No. 40, p. 1940.

Fried, *ibid.* 1913, No. 4, p. 166.

Salomonski, *ibid.* 1913, No. 36, p. 1733.

should he begun tentatively. The same applies to its use in metasyphilitic processes of the brain and spinal cord in which an attack on the nervous system must be avoided.

Fried advises interrupting the treatment already on the appearance of slight secondary effects, as in one case he observed a symptom-complex of secondary effects which showed a surprising similarity to the secondary effects of salvarsan. The first injections were well borne, whereas the last injections frequently produced violent reactions which were identical with embarin and with salvarsan. Only the duration of the syndromes in the case described by the author was shorter than after the use of salvarsan. Nevertheless, he is of opinion that in both instances the same morbid symptoms are present, in which at first the vasomotor paralysis and later injuries of the brain, or of the meninges, preponderate, both caused by the production of anaphylatoxins after acquired susceptibility to embarin.

Emetine Hydrochloride.

The brilliant results obtained by Rogers* with the use of emetine in amœbic dysentery induced G. Baermann and H. Heinemann to investigate Rogers' method. For this purpose they chose specially selected cases which were in particular characterized either by the manner in which the amœbæ were discharged or by the severity of the symptoms. Their results were not so remarkable as those described by Rogers, however, they showed that emetine has a specific action in amœbic dysentery, and doubtless occasional failures which occur will be avoided when the method has been further developed. Certainly these results will not detract from Rogers' achievements in the treatment of amœbic dysentery by emetine. Based on their results, Baermann and Heinemann come to the following conclusions:

1. Emetine is a very powerful amœbotropic drug and amœbocide, which on subcutaneous, and especially on intravenous injection appears to destroy most of all the amœbæ

Rogers, British Medical Journal 1912, I. p. 1424 and II. p. 405. — Merck's Report 1912, p. 178.

* For pharmacological data and the chemical analysis of emetine hydrochloride see: Merck's Wissenschaftliche Abhandlungen No. 17. Baermann-Heinemann, Münchener medizinische Wochenschrift 1913, p. 1132 and 1210.

present in the intestinal wall and floor of the ulcer. Amœbæ which are specially protected are able to escape its action; as far as it at present possible to judge and to demonstrate total destruction of all amœbæ is apparently effected only in rare cases. After ten to seventy days amœbæ are again present, usually, however, in small numbers. Nevertheless, in three cases enormous numbers of young amœbæ were found quite suddenly, so that the impression was gained of a considerable stimulation to segmentation; in another case in the place of the vegetative forms large numbers of cysts suddenly occurred.

2. So far there is no evidence that the cysts are directly destroyed by emetine. Intermittent treatment will possibly be able to prevent their formation in a number of instances. It may be assumed that the few surviving amœbæ migrate from the intestinal wall and under the altered vital conditions prevailing in the intestine and its contents encystment takes place, which would explain the frequent occurrence of cysts.

3. Emetine-fast strains of amœbæ are also known.

4. After repeated injections the ulcers rapidly heal, even in the severest cases ending in death. No amœbæ, or only a very few, are demonstrable in sections. This fact affords an almost conclusive proof of the etiological rôle played by the amœba of dysentery, since with the disappearance of the amœbæ the process, as far as this is anatomically possible, comes to a standstill and heals.

5. Baermann and Heinemann suggest the following method of treatment as being most suitable: One or two intravenous or subcutaneous injections of 0.15 to 0.2 gramme ($2\frac{1}{3}$ —3 grains) of emetine hydrochloride (for intravenous injection the dose is given in 100 c.c. of physiological salt solution). This is followed up during the next eight or ten days by four or five subcutaneous injections of 0.1 to 0.12 gramme ($1\frac{1}{2}$ —2 grains), given at intervals of two or three days, according to the result of examination. This after-treatment should, under certain circumstances, be repeated intermittently, and basing upon their experience, the authors advocate this procedure at intervals of three or four weeks. It is imperative to examine carefully the stools, and this precaution should be observed during a period of several months. The maximum dose for intravenous injection is 0.25 gramme for 60 kilogrammes body-weight.

6. The various brands of emetine at present on the market differ widely as regards activity. — It is apparent from the authors' communications that great importance attaches to the quality and purity of the emetine hydrochloride employed. In some cases they obtained excellent results with Merck's emetine hydrochloride when another make of emetine had proved quite ineffective.

With regard to the secondary effects of emetine injections, Rogers' statements are, on the whole, confirmed by the observations of Baermann and Heinemann. Vomiting occurred only exceptionally after the subcutaneous injection of 0.06—0.15 gramme ($1-2\frac{1}{3}$ grains); otherwise the authors observed only slight discomfort and in a few cases transient, insignificant symptoms of local irritation. If the subcutaneous dose of 0.12—0.15 gramme ($2-2\frac{1}{3}$ grains) was repeated daily, after the third or fourth injection the patient complained of feeling unwell, and there was lassitude with slight vertigo and loss of appetite. On discontinuing the administration of emetine these disturbances disappeared within a short time. Even with large doses no damage was done to the kidneys.

No marked secondary effect became manifest on the intravenous injection of doses of 0.06 to 0.2 gramme ($1-3$ grains), only a slight sensation of giddiness, transient redness of the face or slight nausea were observed. On the other hand, injections of 0.3 to 0.4 gramme ($5-6$ grains) were followed within two to five minutes by general paralysis of the vessels, severe expiratory dyspnoea with apnoea, loss of consciousness with vomiting, the passage of thin stools and excessive slowing of the pulse. Although these symptoms in every case soon passed off, yet the authors regard 0.25 gramme (4 grains) as the maximum dose. Even with these large doses there was no evidence of damage to the kidneys or of any permanent general injury.

In addition to Baermann a number of other authors have recorded their experiences of Rogers' method of emetine treatment. Their reports are briefly reviewed in the following notes.

Marchoux reports two cases of amœbic dysentery in which the use of emetine hydrochloride yielded excellent results and led to a cure. The amœbæ seated in the intestinal mucous membrane were killed by the emetine, whereas the

amœbæ present in the lumen of the intestine were not influenced. For this reason Marchoux advises trials with emetine enemata. However, Chauffard reports a failure with the use of the latter. He had already in one case obtained an appreciable improvement by the use of emetine injections when he gave an enema containing 0.1 gramme ($1\frac{1}{2}$ grains) of emetine hydrochloride. The effect of this treatment was that the number of stools, which under the influence of emetine injections had decreased from fifteen to two a day, now suddenly again increased to fifteen. The enema did not cause any other unwelcome sequelæ. On the other hand, in other cases Chauffard obtained noteworthy successes by the use of emetine injections. In one case, that of a man, aged 28, suffering from chronic dysentery who during a relapse passed at first ten to twelve and later even up to fifty hæmorrhagic stools daily, kosam and tincture of simaruba had been tried without success, whereas already on the second day after the administration of emetine the stools decreased and lost their hæmorrhagic character. Also in the case of a man, aged 40, suffering from dysentery and abscess of the liver, emetine proved effective. After operative removal of the pus 0.04, 0.08, and then a few times 0.04 gramme ($\frac{2}{3}$, $1\frac{1}{4}$ and $\frac{2}{3}$ grain) were injected subcutaneously. A complete cure was rapidly effected without any local or general secondary effects whatever.

Dopter was able to confirm Rogers' statements in many cases of amœbic dysentery. He never injected more than 0.04 gramme ($\frac{2}{3}$ grain) and with this dose he succeeded in effecting an improvement in the patient's general condition, the profuse suppuration disappeared and the other symptoms, such as tenesmus, colic and hæmorrhagic stools were improved. Basing upon his extremely satisfactory results, he advocates emetine treatment in warm countries where this disease annually claims a large number of victims.

Dufour, in a man aged 26, observed a decrease in the number of stools passed from twelve to two after the ad-

Chauffard, *Revue de thérapeutique* 1913, No. 14, p. 481. — *Semaine médicale* 1913, No. 12, p. 141. — *Presse médicale* 1913, No. 31, p. 308, No. 32, p. 317 and No. 39, p. 389.

Dopter, *Semaine médicale* 1913, No. 11, p. 129 and No. 15, p. 179. — *Presse médicale* 1913, No. 32, p. 317.

Dufour, *Semaine médicale* 1913, No. 16, p. 190.

ministration in all of 0.3 gramme (5 grains) of emetine hydrochloride.

Flandin and Dumas, in a case associated with abscess of the liver, after opening the abscess, gave a subcutaneous dose of 0.08 gramme ($1\frac{1}{4}$ grain), and then two injections of 0.04 gramme ($\frac{2}{3}$ grain) of emetine hydrochloride, and repeated this treatment after some time with a few injections of 0.08 gramme ($1\frac{1}{4}$ grain) and obtained a complete success.

R. L. Spittel advocates the use of emetine in particular in cases of amœbic dysentery associated with abscess of the liver. He states that it destroys the amœbæ if it is injected into the abscess cavity after aspiration of the pus; in addition it is apparently capable of promoting cicatrization.

Rouget prescribed emetine in two cases, Brailion in one case of chronic amœbic dysentery. A cure was effected already within the course of a few days. Rouget was also able to confirm the excellent action of emetine in a case associated with abscess of the liver, and he therefore advises that such patients, who may have to undergo an operation later on, should undergo a preliminary treatment with emetine. He believes that in such cases emetine at least displays a curative after-effect.

In a case of a year's standing Dufour and Thiers gave subcutaneously within a period of eight days 0.3 gramme (5 grains), and then 0.12 gramme (2 grains) rectally. The patient improved markedly, although this treatment did not succeed in completely eradicating the amœbæ. R. E. Cloud, too, reports a case of amœbic dysentery which was successfully treated by injections of emetine.

Gaïde and Mouzels report four cases observed by themselves. They were all cases of chronic dysentery which were appreciably improved by emetine treatment. However, the authors did not succeed in obtaining a definite cure.

Flandin-Dumas, *Presse médicale* 1913, No. 32, p. 317. — *Semaine médicale* 1913, No. 11, p. 129.

Spittel, *British Medical Journal* 1913, II, p. 1058.

Rouget, *Semaine médicale* 1913, No. 18, p. 214. — *Presse médicale* 1913, No. 32, p. 317.

Brailion, *Revue de thérapeutique* 1913, No. 14, p. 481.

Dufour-Thiers, *Presse médicale* 1913, No. 32, p. 317.

Cloud, *Journal of the American Medical Association* 1913, Vol. 59, p. 1899.

Gaïde-Mouzels, *Presse médicale* 1913, p. 640.

Lyons treated six cases with subcutaneous injections of emetine, and in five obtained a rapid success. Until the stools became normal this treatment required from two to twenty days; the largest single dose of emetine hydrochloride injected was 0.045 gramme ($\frac{2}{3}$ grain), and the average total amount given was 0.15 gramme ($2\frac{1}{3}$ grains). Compared with the internal administration of ipecacuanha this method has the advantage that it is simple, permits of accurate dosage, yields reliable results, and does not cause vomiting or depression.

Milian treated a patient suffering from amoebic dysentery and syphilis. As the dysentery disappeared after four injections of salvarsan, he now tried to influence the syphilitic affection by means of emetine, but in this, according to his report, he was unsuccessful. Within forty-eight hours and after four injections of 0.01 gramme ($\frac{1}{6}$ grain) of emetine hydrochloride the episcleritis and the headaches disappeared. In a tabetic patient, too, the relapses which had resisted mercurial and salvarsan treatment are said to have been very beneficially influenced by injections of emetine. The author, however, is of opinion that a successful result of this kind is dependent on a preliminary specific course of treatment.

Allen C. Hutcheson reports thirteen cases of amoebic dysentery, partly acute and partly chronic forms, in which he gave twice a day a subcutaneous injection of 0.02 gramme ($\frac{1}{3}$ grain) of emetine hydrochloride. In seven cases in which the presence of amoebæ was positively demonstrated the stools were free from blood at the latest after six days, in some cases already after one day, and the majority of the patients were discharged from the hospital cured after six days. One case which showed no amoebæ became free from symptoms after seven days. Of two cases of amoebic infection in which *Schistosoma japonicum* was also present, the one, a patient who passed daily from ten to fifteen stools and who showed extreme emaciation, showed no improvement after eight days; the other, who had suffered from dysentery for four years and frequently passed a large number of stools, often containing blood, and also had an enlarged spleen, became free from amoebæ and the stools from blood after

Lyons, Journal of the American Medical Association 1913, Vol. 60, p. 1216.

Milian, Semaine médicale 1913, No. 12, p. 141.

Allen C. Hutcheson, China Medical Journal 1913, p. 243.

five days' treatment. This finding was again confirmed after thirty days, while the patient's condition was very good. *Schistosoma* infection alone was present in three cases; of these two showed no blood after six days' emetine treatment, while one showed no improvement after seven days. The author does not attempt to draw a definite conclusion as to the value of this treatment in *Schistosoma* dysentery from his results; however, he feels justified in advising a further trial of the method. On the other hand, his experience shows that the specific action of emetine in amoebic dysentery is beyond doubt*.

Couteaud, who describes some cases of amoebic dysentery and their treatment with emetine, comes to the conclusion, based on his observations, that abscesses of the liver should not be treated either surgically or with emetine, but that they should be treated by both methods simultaneously. Purely surgical treatment still shows too high a percentage of deaths, and treatment by emetine alone does not always yield the desired result.

Valence has treated a chronic case of dysentery-like inflammation of the rectum (rectitis) by emetine. The patient had already been treated without success with various drugs, as his health was seriously impaired by syphilis and typhoid fever. In the beginning he was given a daily intramuscular injection of 0.08 gramme ($1\frac{1}{4}$ grain), then, as these proved painful, subcutaneous injections of 0.02 to 0.1 gramme ($\frac{1}{3}$ to $1\frac{1}{2}$ grains), which were borne without pain. It appears that the successful issue was due to the larger doses, for after two days no amoebæ could be demonstrated in the rectum. Neither did they reappear, and by means of the rectoscope the author found that healing was gradually progressing.

G. Low and Mallannah have given emetine internally with successful results. Low administered it in the form of keratinized tablets containing 0.03 gramme ($\frac{1}{2}$ grain), and already after two days he observed an improvement without

* Mention may also be made of the papers by S. R. Douglas (British Medical Journal 1913, II, p. 1282) and K. Hintze (Archiv für Schiffs- und Tropenhygiene 1913, No. 17).

Couteaud, Gazette médicale de Paris 1913, p. 269.

Valence, Bulletin médical 1913, No. 49. — Revue de thérapeutique 1913, No. 20, p. 706.

Low, British Medical Journal 1913, No. 2739, p. 1369.

Mallannah, British Medical Journal 1913, No. 2736, p. 1206.

any secondary effects. In his opinion the tablets are in some cases to be preferred to injections, however, it must be taken into account that in the event of no action becoming manifest they may have passed the digestive tract unaltered. Mallannah gave emetine by mouth in an aqueous solution to a woman, aged 40, an alcoholic, whose abscess of the liver was punctured. In spite of existing fever, weakness, emaciation, nausea and refusal to take food the author prescribed three times a day 0.015 gramme ($\frac{1}{4}$ grain) of emetine hydrochloride in aqueous solution. In the course of a week the temperature returned to normal, the appetite was restored and the other symptoms disappeared. The patient also gained in weight and was cured after taking 1.35 gramme (20 grains) of emetine.

The experiments undertaken by Valassopoulos with emetine in hæmorrhage and hæmoptysis were doubtless based on the fact, long known, that ipecacuanha also displays a styptic action on internal hæmorrhages. The author records a case of carcinoma of the rectum in which he succeeded in quickly checking the bleeding by injections of 0.02 gramme ($\frac{1}{3}$ grain) of emetine hydrochloride. This treatment is said to prove useful also in hæmoptysis of tuberculotics. The basis of the styptic action of emetine has not yet been established.

A contribution by Ch. Flandin also refers to the use of emetine hydrochloride in hæmoptysis. This author obtained a striking success in tuberculous hæmoptysis with subcutaneous injections of 0.04 gramme ($\frac{2}{3}$ grain). If this dose is injected into a patient during an attack of spitting of blood the hæmorrhage is immediately arrested, without causing any unpleasant sensation whatever. The patient who was spitting blood while sitting or lying on his side is able to turn over and breathe without trouble. In very severe cases the hæmoptysis reappears and for this reason the patients should be kept for some time under the action of emetine. To this end an injection is made during the attack and is repeated twelve hours later, and again on the following day; if necessary a fourth and fifth injection are given on the following days. With this treatment it is said that in almost every case the hæmoptysis can be checked, in some instances even per-

Valassopoulos, Bulletin et mémoires de la société médicale des hôpitaux 1913, p. 1008.

Flandin, Presse médicale 1913, No. 78, p. 779.

manently. Flandin is unable to offer an explanation for the action of emetine, and according to his investigations it is neither attributable to an influence on the blood pressure nor to any property of the drug of increasing the coagulability of the blood.

It may be mentioned that T. H. Delany was led to try ipecacuanha in cholelithiasis on the basis of his successes with this drug in the treatment of dysentery associated with hepatitis, and he found that it proved markedly useful, particularly in inoperable cases. If vomiting is produced by the large doses which are required the author advises a trial with subcutaneous injections of emetine.

Erepton.

In view of the importance which rectal feeding has assumed of recent years, a contribution by G. Avé Lallemand and O. Gross dealing with the value of erepton* is of interest. The authors have proved by experiments that the internal administration of this preparation to healthy persons does not cause any disturbance of nitrogen metabolism, on the contrary, it is well absorbed and favours the retention of nitrogen. Therefore, in suitable cases erepton may be taken into account as a preparation with a high food value, or as an addition to nourishment. The rectal use of this preparation is, however, especially valuable, provided this form of application is well borne, because the authors found that the rectal administration of erepton solutions was not quite devoid of irritant action, in contradistinction to statements by other observers. Indeed, a large number of their experiments failed owing to the inability of the patients to retain the erepton enemata for even a few minutes. This was even more frequent in sick persons than in healthy individuals. Nevertheless, the authors are of opinion that a trial should always be made with the rectal use of erepton whenever this course is indicated. If it is not tolerated in the form of an erepton-maltose enema, then a combination with the hitherto customary nutrient enemata is indicated.

Another possible field of application of practical importance may be found in those cases in which there is

Delany, Indian Medical Gazette 1913, p. 180.

Lallemand-Gross, Therapeutische Monatshefte 1913, No. 2, p. 127.

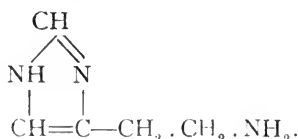
* Compare Merck's Report 1911, p. 228.

a serious disturbance of the entire albumin digestion. In a patient with severe chronic degeneration of the pancreas erepton proved an excellent remedy, and this result points to its being an indispensable preparation in severe affections of the pancreas. The patient, who in spite of a generous supply of nitrogen showed constant deficiency of nitrogen, on two days was given only milk and on the following two days milk which was in part substituted by erepton, at the same time the fat and milk sugar contained in the amount of milk not administered were given as well. With this treatment it was possible to restore the patient's nitrogen balance. A further indication for erepton may be afforded by insufficiency of the pancreas, which is manifested by gastric disturbance known as anacidity or hypoacidity.

Ergot of Rye.

The investigations of Barger and Dale have contributed very considerably to our knowledge of the active principles of ergot*, and now the synthesis of these bodies is claiming greater attention. These two authors succeeded in demonstrating the presence of three bases, ergotoxine, iminazolyethylamine and para-oxyphenylethylamine, in ergot and in alcoholic or aqueous extracts of this drug. Ergotoxine appears to be the toxic principle, or at least the most toxic component of ergot and is apparently the causal agent of the so-called ergot gangrene. It possesses not only an ecboic action on the uterus but also a vaso-constrictor effect and consequently increases blood pressure. Owing to its secondary effects it is for the present not likely to come into consideration as a substitute for ergot. On the other hand, the other bases, especially iminazolyethylamine, are likely to be extensively used in gynæcological practice.

β -iminazolyethylamine (histamine, ergamine) is produced by the splitting off of carbonic acid from histidine and has the following chemical formula:



* Compare Merck's Report 1912, p. 182 and H. H. Dale, Journal of Physiology 1913, Vol. 46, p. 291.

Its pharmacological and therapeutic action was described during the past year by M. Guggenheim, H. Eppinger, W. Einis, Oehme, H. G. Barbour, H. Fühner, F. Jäger and C. Koch.

According to Einis, who made a comparative study of the pharmacological action of pituitrin and histamine, histamine has a more powerful effect on the heart's action, hence the author advocates its trial, in addition to pituitrin, in cardiovascular disturbances. Compared with pituitrin, he states, it has the advantage of being a pure chemical body of uniform composition. Fühner has already made the same recommendation, and in a recent communication he states that in experiments on animals 0.5 milligramme of histamine hydrochloride exhibits approximately the same action as 1 c. c. of pituitrin*.

Oehme found that histamine displayed no toxic symptoms on injection into the portal vein or when slowly infused into the jugular vein, and that it very soon disappears from the blood without appearing in the urine.

Barbour compared the action of histamine with that of adrenalin and came to the conclusion that adrenalin dilates the coronary vessels in contradistinction to its action on the other blood vessels, whereas histamine displays a constrictor action also on the coronary vessels. Therefore, unlike adrenalin, it cannot be regarded as a universal "sympathomimetic" remedy.

Jäger has tried it in women; he employed a 0.2 p. c. solution of iminazolyethylamine which he injected subcutaneously or intramuscularly in doses of 2 to 4 c. c. Especially the large doses proved capable of stimulating the functions of labour pains and hastened delivery. However, in view of the secondary effects observed by the author caution is

Guggenheim, *Therapeutische Monatshefte* 1913, No. 7, p. 508.

Eppinger, *Wiener medizinische Wochenschrift* 1913, No. 23.

Einis, *Biochemische Zeitschrift* 1913, Vol. 52, p. 96.

Oehme, *Archiv für experimentelle Pathologie* 1913, Vol. 71, p. 76.

Barbour, *Journal of Pharmacology and Experimental Therapy* 1913, Vol. 4, p. 245.

Fühner, *Therapeutische Monatshefte* 1913, No. 3, p. 202.

Jäger, *Zentralblatt für Gynäkologie* 1913, No. 8, p. 265.

Koch, *ibidem* 1913, No. 16, p. 564.

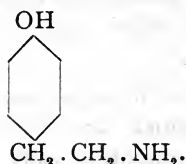
* Compare Merck's Report 1912, p. 324.

necessary in using this preparation as an ecboic. On the other hand, there is no objection to its use during parturition where only very small doses are required. Here it acts as a complete substitute for ergot since it yields the same results as the latter.

Koch's experiments with iminazolyethylamine in obstetrics include its use in childbed and also during delivery. In childbed he gave the preparation only per os in doses of six to twenty drops, thrice daily, of a 0.2 p. c. solution. He found that the larger doses did not produce any better results than the smaller ones. No secondary effects were observed, only the multiparæ complained more frequently than usual of painful after-pains. The action was uniformly good. During delivery he gave the preparation subcutaneously, but never exceeded a dose of 1 c. c. of the above mentioned solution, in order to avoid any unpleasant surprises. Usually, labour was beneficially influenced and only in three out of twenty-five cases the injection failed entirely. The author hopes that a combination of β -iminazolyethylamine and para-oxyphenylethylamine will prove a useful substitute for extracts of hypophysis and ergot; tenosin is a preparation of this kind (compare below).

An observation of Eppinger is of theoretical importance for the production of urticaria. If a few drops of a 1 in 1000 histamine solution are applied to a slight fissure of the skin, which is not bleeding, it becomes blanched within a few minutes. The blanching extends along the course of the fissure and a wheal-like elevation of the skin forms which resembles genuine urticaria and causes an itching sensation. If 0.5 to 1 c. c. of this solution is injected subcutaneously the same symptoms appear at the site of injection. Moreover, in some cases the face, hands, feet, abdomen and thighs exhibit superficial red patches resembling typical urticaria. If it is borne in mind that histamine is a degradation product of albumin, which under circumstances is formed in the intestine and which has been found in the intestinal mucous membrane and in the stools in diarrhœa, there is some justification for regarding histamine as the causal agent of urticaria, should this body be formed in the course of atypical intestinal fermentations.

Oxyphenylethylamine (para-), which is also known under the name of "uteramin, systogen, or tyramin", has the chemical formula:



For therapeutic use the chloride alone deserves consideration, the same as with histamine. Further particulars will be found in my last year's Report (p. 182—183). Recently this preparation has been placed on the market under the name of "uteramin" in sterile ampoules of 1·2 c. c. (= 0·01 gramme of active substance), and in tablets for internal administration, each containing 0·01 gramme of active substance, and in 1 p. c. solution, also intended for internal use. For subcutaneous injection it is given in doses of 0·5 to 1 c. c. (maximum daily dose = 3 to 4 c. c.) of the preparation issued in ampoules, internally 15 to 30 drops of the 1 p. c. solution are given thrice daily, or three to four tablets a day.

Ertel, A. Bickel and M. Pawlow, and J. Lauffs have recently reported on the use of uteramin. According to these authors it is indicated in atony of the uterus and during the third stage of labour. Its use in rhinology in hæmorrhages, reported on by Lauffs, is new; he states that it proved useful in bleeding from the nose in which it was used either in the form of subcutaneous injections (1 c. c.) or of pledgets of cotton wool dipped in uteramin solution. It is also useful as a prophylactic before nasal operations. According to this author an injection of 1 c. c. prevents the occurrence of profuse bleeding.

Tenosin is a combination of the two above mentioned substances, β -iminazolyethylamine and para-oxyphenylethylamine. It is issued in aqueous solution (also in ampoules of 1·2 c. c.) in the strength suitable for therapeutic use. F. Jäger, R. Zimmermann and Krosz report on this preparation.

Ertel, Wiener klinische Wochenschrift 1913, No. 6, p. 239.

Bickel-Pawlow, Biochemische Zeitschrift 1912, Vol. 47, p. 435.

Lauffs, Deutsche medizinische Wochenschrift 1913, No. 46, p. 2252.

Jäger, Münchener medizinische Wochenschrift 1913, No. 31, p. 1714.

Zimmermann, ibidem 1913, No. 48, p. 2675.

Krosz, Zentralblatt für Gynäkologie 1913, No. 43, p. 1587.

Jäger found that a solution containing in 1 c. c. 0.0005 gramme of iminazolyethylamine and 0.002 gramme of oxyphenylethylamine was the most suitable mixture since the very small amount of iminazolyethylamine it contains excludes any action referable to its dangerous constituent. The effect of the preparation is best seen after the expulsion of the placenta. In most cases one subcutaneous injection of 1 c. c. is sufficient, if not, this dose may be repeated after some time. According to Jäger, tenosin is a useful substitute for ergot because it closely approaches the latter's complex action and owing to the small dosage secondary effects are excluded*. On the other hand, it is superior to the preparations of ergot hitherto in use in that it acts more promptly and quicker, and this may prove important in atonic hæmorrhages. However, Zimmermann did not find that tenosin displayed a quicker or more sustained action than extract of ergot. Nevertheless, in his opinion it fulfils its object if its action closely approaches or equals that of ergot. The author seeks the advantages of this preparation in its being an absolutely constant, stable compound, the composition and mode of action of which are known and can be controlled, and which is free from those substances which are present in ergot and which give rise to dangerous toxic symptoms and which lower the blood pressure.

According to Krosz, tenosin is a harmless ebolic the action of which equals that of ergot. Indeed, it is superior to the latter as regards rapidity and activity. However, as is the case with ergot, occasionally it may fail. On the other hand, the author gained the impression that on the whole the action of tenosin does not last as long as is the case with preparations of ergot. Krosz also prescribed tenosin in a few cases during childbed. The administration of 20 drops three times a day yielded satisfactory results in that involution of the uterus took place satisfactorily under powerful contractions. Tenosin should also prove a useful substitute for ergot in the treatment of abortion.

Ernutin is a combination of β -iminazolyethylamine, para-oxyphenylethylamine and ergotoxine, and is also issued in solution. It is recommended in the treatment of post-partum hæmorrhages, Graves's disease, hysteria, diabetes insipidus,

* Compare W. Lindemann, Berliner klinische Wochenschrift 1913, No. 44, p. 2042.

enuresis and spermatorrhœa. It is given in subcutaneous doses of 0.3 to 0.6 c. c., to be repeated if necessary, or by mouth in doses of 2 to 3.5 c. c., every three hours*.

Mention may be made of *erystypticum* "Roche", which has been discussed by A. Hirschberg, A. Gisel, E. Keibel and Katz. It is a combination of *hydrastinine*, extract of *hydrastis* and *secacornin*** and thus combines the actions of *hydrastis* and *ergot*. The preparation, which is supplied in a solid as well as liquid form, is given internally in gynæcological practice as a *styptic* in all cases of pathological hæmorrhage from the genitals, and also in hæmorrhages from the nose, stomach, bladder and kidneys; further, in Graves's disease, aortic insufficiency, serum disease, bronchial asthma, mucous colitis, pollutions and nocturnal enuresis. The single dose is 15 to 20 drops, or a corresponding amount of the solid preparation.

Ervasin.

The principal indications for *ervasin-calcium****, according to M. Richter, are acute articular rheumatism, neuralgias accompanied by severe pains, and influenza. The author recommends the use of not too small doses, and as in his experience it is free from secondary effects and experiments have shown that it is harmless even in large doses, it may be given in daily doses of 6 to 8 grammes (90—120 grains) in severe pains. Usually, however, three doses of 1 gramme (15 grains), or four or five doses of 0.5 gramme ($7\frac{1}{2}$ grains) daily are sufficient. Children and aged persons are given correspondingly smaller amounts.

R. Topp used *ervasin-calcium* with successful results in the lightning pains of tabes. The preparation may also prove

* Compare *Pharmazeutische Zentrallhalle* 1908, p. 796. — *Pharmaceutical Journal* 1907, p. 24. — *Vierteljahresschrift für praktische Pharmazie* 1908, p. 232.

Hirschberg, *Medizinische Klinik* 1912, No. 40, p. 1629.

Gisel, *Deutsche medizinische Wochenschrift* 1913, No. 22, p. 1046.

Keibel, *Deutsche medizinische Wochenschrift* 1913, No. 6, p. 269.

Katz, *Medizinische Klinik* 1913, No. 17, p. 670.

** *Secacornin*, formerly called "*Ergotin Keller*", see Merck's Report 1900, p. 93.

*** Compare Merck's Report 1912.

Richter, *Klinisch-therapeutische Wochenschrift* 1913, No. 25, p. 750.

Topp, *Deutsche Medizinal-Zeitung* 1913, No. 18, p. 312.

useful as a symptomatic in hemicrania and cephalalgia, provided a causal treatment is indicated.

Ether.

M. Guibé discusses the value of intramuscular ether anæsthesia. He directs that before making the injection the patient's eyes should be covered with a black cloth, whereupon amounts of 10 to 20 c. c. are injected into different parts of the gluteal musculature, taking care to avoid injury to a vein, and using a suitable syringe with a capacity of 20 to 50 c. c. The total dose is based upon the patient's weight, using 1 gramme of ether for each kilogramme of body-weight. However, the nature of the operation and the duration of anæsthesia required must be taken into account, as well as individual susceptibility since under certain circumstances an amount which produces toxic symptoms in susceptible persons may in less sensitive individuals produce an insufficient degree of anæsthesia. Anæsthesia by means of intramuscular injections of ether is therefore not reliable, although it has been recommended also by other authors.

Of greater promise is the intratracheal insufflation of ether, a method inaugurated by A. Ehrenfried and which is said to be especially useful in operations upon the thorax, and also in operations about the mouth, throat, face and head, while being free from unwelcome sequelæ. The author extols the calmness of the anæsthesia induced by this method as well as its harmlessness. R. E. Kelly was able to confirm its usefulness.

The intravenous injection of ether, with or without the simultaneous injection of isopral, as proposed by Burkhardt, is, according to W. Graef's report, also an effective method of inducing anæsthesia. The author found it especially suitable for operations on the head and throat. He never used more than 200 c. c. of isopral solution (3 grammes of isopral) and never saw any bad after-effects, and among 360 cases slight excitation occurred in 20 and marked excitation in 4 cases. With proper technique no infections and no embolism occur.

Guibé, *Journal des praticiens* 1912, No. 44.

Ehrenfried-Kelly, *British Medical Journal* 1912, II, p. 616 and 617.

Burkhardt, *Merck's Report* 1911, p. 231.

Graef, *Beiträge zur klinischen Chirurgie* 1913, Vol. 83, No. 1.

Recently K ü m m e l again recommends the intravenous use of ether.

The use of ether in the place of chloroform as an anæsthetic is suggested in operations in acute inflammatory processes in the abdominal cavity, for, according to S p r e n g e l, in these cases chloroform may induce a condition known as post-operative sepsis, and which consists in jaundice, restlessness, sleepiness and coma, and usually ends fatally. His experience in operations for appendicitis also induced M e i s e l to abandon the use of chloroform in favour of ether. In this connexion reference may be made to a report by E. A. G r a h a m, in which the value of giving fat after ether anæsthesia is discussed. The author found that the administration of fats and oils after anæsthesia is capable of stimulating phagocytosis; fats are also said to prevent the absorption of ether in the gastrointestinal tract.

A statement by S o u l i g o u x appears to have excited considerable interest. This author reports that he has used ether with very good results as a preventive of infection in wounds and operations. He records, inter alia, one case in which owing to contused wounds of the legs a double amputation was to be performed but was refused. The wounds were dressed with ether and a plaster of Paris bandage applied, with the result that the wounds healed. In whitlows, phlegmons and lymphangitis, after cleansing with soap and water, the author applied ether compresses and obtained satisfactory results by this method, the value of which was also confirmed by C u n é o. The use of ether in peritonitis is specially deserving of attention. In an alarming case of generalized peritonitis from perforation, after closing the perforation, Souligoux removed the pus and intestinal contents present in the peritoneal cavity by washing it out with plenty of ether and then closed the abdomen, inserting a drain. This case healed. T e m o i n obtained the same satisfactory result

Kümmel, Zentralblatt für Chirurgie 1913, No. 28, Beilage p. 57.

Sprengel, Meisel, Zentralblatt für Chirurgie 1913, No. 28, Beilage p. 57 and 58.

Graham, Transactions of the Chicago Pathological Society 1913, Vol. 9, p. 49.

Souligoux, Bulletin de la société de chirurgie 1913. February 19, Klinisch-therapeutische Wochenschrift 1913, No. 21, p. 648.

Temoin, Morestin, Souligoux, Münchener medizinische Wochenschrift 1913, No. 33, p. 1860.

in two complicated cases, and he considers ether the most reliable agent for combating post-operative peritonitis. Dergane also advocates the ether method as by it he successfully treated two cases of peritonitis from perforation. Morestin remarks that he has used the ether method with successful results already since 1901.

By means of animal experiments M. Kochmann found that a mixture of chloroform and ether in a definite proportion produced an intensified narcotic action. Whereas mixtures of ether and chloroform in which the ratios $2+1$, $4+1$ and $8+1$ existed only exhibited a summation of the narcotic action, a mixture of 1 part of chloroform and 6 to 7 parts of ether displayed a more intense action than that corresponding to the summation of the actions of the single components of this mixture. Hence this mixture deserves a further trial in operative practice.

Ethyl Chloride.

A. Kneucker reports on the use of ethyl chloride in dental operations. In an investigation of Kulenkampff's* method of ethyl chloride anæsthesia he found that care must be taken in the technique of its application, and in his experience the following procedure has proved most effective: The operation is performed on the patient sitting in the dental chair slightly tilted back, and the patient is directed to open his mouth wide and breathe deeply. The bottle of ethyl chloride is now opened and a slightly bent glass tube about 0.5 cm. in diameter and 10 cm. in length is attached so that the bottle gives out its contents in drops. With his left hand the operator holds the piece of gauze placed over the patient's mouth and nose and at the same time lightly presses on the alæ nasi to close the nostrils so that the patient is made to breathe principally through the mouth. The bottle of ethyl chloride is held in the right hand and the fluid is

Dergane, Wiener klinische Wochenschrift 1913, p. 1332. — Zentralblatt für Gynäkologie 1913, No. 46, p. 1705.

Morestin, Semaine médicale 1913, No. 21, p. 248.

Kochmann, Deutsche medizinische Wochenschrift 1913, No. 40, p. 1934.

Kneucker, Wiener klinische Wochenschrift 1913, No. 31, p. 1277.

* Compare Merck's Report 1911, p. 237.

dropped on to the gauze. The number of drops is accurately counted and dosed, according to Kulenkampf's directions. The gauze is removed as soon as unconsciousness sets in. Keeping the mouth open has the advantage that the operation can be begun immediately and no time is lost, for the rapid onset and brief duration of anæsthesia make every second of value. With children the ethyl chloride may be applied by means of the mouth mirror, by moistening it with ethyl chloride and holding it in front of the open mouth.

For inducing anæsthesia in dental operations (extractions) G. Bardet employs a mixture of 60 parts of ethyl chloride, 35 parts of methyl chloride and 5 parts of ethyl bromide. Inhaled with sufficient air this mixture produces quiet sleep within less than two minutes, without any excitement, and after one minute the patient awakens with at the most a slight sensation of nausea. As an adjuvant the author used opium deprived of its morphine as this preparation displays a good sedative action without producing a more prolonged narcotic effect. In addition he also gave a little calcium carbonate to prevent the possibility of hyperchlorhydria.

Schwarz recommends ethyl chloride anæsthesia for all operations lasting only a short time and in which complete anæsthesia is not required, but only a condition of intoxication. His results were without exception satisfactory and he never observed any secondary effects. He used the commercial preparation supplied in bottles with a metal cap and allowed the contents to drop on four layers of gauze placed over the patient's mouth and nose.

On the other hand, A. Falk states that in operations on the palatine and pharyngeal tonsils, incision of abscesses of the mouth, paracentesis, etc., in children full anæsthesia is required, as in these cases the analgesic stage is not of sufficient duration. He considers it quite safe, as out of 500,000 cases only fourteen deaths are recorded. He states that the onset of anæsthesia is recognizable by muscular relaxation, convergence of the eyes, extreme dilatation of the pupils, and deep, stertorous breathing.

Bardet, *Presse médicale* 1913, No. 45, p. 451.

Schwarz, *Berliner klinische Wochenschrift* 1913, No. 22, p. 1037.

Falk, *Zeitschrift für Laryngologie, Rhinologie und ihre Grenzgebiete* 1913, Vol. 6, p. 1.

Based on the results of his pharmacological investigation of ethyl chloride, R. König draws the following conclusions regarding its suitability for inducing anæsthesia: The rapid onset of analgesia and the brief duration of anæsthesia make ethyl chloride appear a suitable anæsthetic for short operations, e. g., in dental work, provided proper technique is adopted and the necessary precautions are taken and only a single small dose is used. It is, however, useless for longer operations as here larger amounts are required which would entail the danger of suffocation. It must be borne in mind that in spite of its comparative harmlessness ethyl chloride, owing to the constant presence of dyspnœa and the considerable fall in blood pressure, is not an indifferent anæsthetic. In the author's opinion ethyl chloride is preferable and less dangerous when used as a local anæsthetic than for inducing even the shortest anæsthesia.

H. Seidelin obtained very good results in epithelioma of the skin by freezing with ethyl chloride. His method consists in freezing the epithelioma for a period of two to seven minutes by spraying it with ethyl chloride, repeating the procedure at several sittings. Two cases remained free from recurrences for five years.

Ethyl Hydrocupreine (Optochin Hydrochloricum).

The fact that animal experiments* have shown that pneumococci are acted upon by ethyl hydrocupreine suggested the possible use of this preparation in *ulcus serpens corneæ*. A basis for the elucidation of this question is afforded by the observations of S. Ginsberg and M. Kaufmann who made experiments on rabbits' eyes. They found that a 0.5 p. c. solution of ethyl hydrocupreine after twenty-four hours' action displayed a pronounced curative effect on the infection and on the intra-corneal pneumococci, and was non-injurious to living tissue. It remains to be seen whether these findings are confirmed when the preparation is tried on the human eye and this must be established by clinical trials. Both authors are of opinion that it is highly probable that a

König, Archiv für klinische Chirurgie 1913, Vol. 99, No. 1.
Seidelin, Lancet 1913, I, p. 1663.

* Compare Merck's Report 1912, p. 188.

Ginsberg-Kaufmann, Klinische Monatsblätter für Augenheilkunde 1913, Vol. 51, p. 805.

solution of ethyl hydrocupreine will prove even more useful when applied to the human eye, or in *ulcus serpens corneæ*, than is apparent from animal experiments; however, the strength of the solution to be used and the time it should be allowed to act still await investigation*.

The anæsthetic action of ethyl hydrocupreine was discussed in last year's Annual Report. More light is thrown upon this subject by the further reports of the results of their experiments published by J. Morgenroth and S. Ginsberg. These authors were able not only to confirm the powerful anæsthetising effect of ethyl hydrocupreine, but they also found that the higher homologues of the series, such as propyl hydrocupreine, isopropyl hydrocupreine and isoamyl hydrocupreine, have a still greater anæsthetising power, and the investigations of the authors show that, for instance, isoamyl hydrocupreine is at least twenty to twenty-five times more effective than cocaine. The anæsthetic action of these substances does not appear to be limited to the cornea, but seems capable of proving useful for infiltration anæsthesia. E. Ungér has used a 0.2 p.c. solution with adrenalin in *herniæ*, varices, tumours, etc., in doses up to 500 c.c. Anæsthesia sets in somewhat later than with a solution of novocaine and adrenalin, but it appears to last longer. The author found that the preparation possesses two important advantages — the above mentioned solution can be given in larger doses than the novocaine-adrenalin solution, and the after-pains are slighter than after novocaine-adrenalin. Isoamyl hydrocupreine cannot be used without the addition of adrenalin, as it produces a disturbing degree of hyperæmia. The author advocates further trials on a more extensive scale in order to confirm his results.

Reports on the pharmacological action of ethyl hydrocupreine have also been published by Th. Engwer and

* A. Leber has already made trials with an oily suspension of ethyl hydrocupreine and an aqueous solution of ethyl hydrocupreine hydrochloride and has obtained very satisfactory results in *ulcus serpens*. *Medizinische Klinik* 1913, No. 24, p. 969. Morgenroth-Ginsberg, *Berliner klinische Wochenschrift* 1913, No. 8, p. 343.

Unger, *Berliner klinische Wochenschrift* 1913, No. 4, p. 180.

Engwer, *Zeitschrift für Hygiene und Infektionskrankheiten* 1912, Vol. 73, p. 194.

K. E. Boehncke. Engwer was able to confirm the marked chemotherapeutic action of ethyl hydrocupreine on experimental pneumococcal infection, already demonstrated by Morgenroth and Levy. His experiments on mice and guinea-pigs showed that according to the severity of the infection the percentage of animals which were saved by this treatment varied, whereas all the control animals which received no treatment died. The author ascribes the action to the extracellular destruction of the pneumococci, and not to a possible stimulation of phagocytosis. With regard to the toxic action of the preparation, this appears to show individual variations and to depend upon the outside temperature. Further, the author draws attention to the fact that ethyl hydrocupreine and pneumococcus serum reciprocally assist each other in their action. Boehncke has studied this question more thoroughly, and he found that while either ethyl hydrocupreine or pneumococcus serum alone was able to prevent the death of the experimental animals in the ratio of only 11 p.c., with the same doses 83 p.c. of the animals were saved by a combination of both remedies. If the administration of both preparations was made simultaneously with the infection the result was still better.

Therapeutic trials have been undertaken by H. J. Vetlesen, Lenné and Parkinson. Vetlesen gave 0.5 gramme ($7\frac{1}{2}$ grains) of ethyl hydrocupreine by mouth three times a day in pneumonia, and he found that the course of the affection to the critical or lytic point was marked by special rapidity. In three cases deverification occurred before the expiration of forty-eight hours, in two cases after two and a half days, in two cases after four days and in one case after eight days. According to Vetlesen, success depends upon the early administration of the drug.

Parkinson obtained negative results with the use of internal and subcutaneous doses of 0.5 to 2 grammes ($7\frac{1}{2}$ to 30 grains) in croupous pneumonia; at least he was unable to observe any beneficial influence on the course of the

Boehncke, Münchener medizinische Wochenschrift 1913, No. 8, p. 398.

Morgenroth-Levy, Berliner klinische Wochenschrift 1911, No. 34 and 44.

Vetlesen, Berliner klinische Wochenschrift 1913, No. 32, p. 1473.

Lenné, Berliner klinische Wochenschrift 1913, No. 43, p. 1984.

Parkinson, Zeitschrift für Chemotherapie Vol. 2, No. 1.

affection. Whereas Vetlesen reports the absence of undesirable secondary effects, Parkinson observed dilatation of the pupils after the administration by mouth of 1 gramme (15 grains) and the subcutaneous injection of 0.5 gramme ($7\frac{1}{2}$ grains).

On the other hand, Lenné's experiments prove beyond doubt that ethyl hydrocupreine displays a specific effect in pneumococcal infection and in pneumonia. The author prefers intravenous injection, which in his experience is very well borne.

J. Morgenroth and J. Tugendreich state that a combination of ethyl hydrocupreine and sodium salicylate is especially useful in trypanosome infection. A combination of both drugs with small doses of salvarsan is also said to yield remarkably good results. The authors consider this combination to be worthy of note in the treatment of man, as with it the use of large doses of salvarsan, which under circumstances are dangerous, may be avoided.

Eucalyptol.

Some years ago Berliner proposed a method of treating tuberculosis and bronchitis which is based upon the intramuscular injection of eucalyptol and menthol. Recently he has reported the results of his further investigations. The liquid for injection is prepared by dissolving 10 grammes of menthol in 20 grammes of eucalyptol and adding to the solution 50 grammes of oleum dericini. The author gave ten injections of 1 c.c. of this solution every second day, then ten injections at intervals of two days and the following ten injections at intervals of three days. The injections are said to be painless if pure drugs are employed. Occasionally sensibility to pressure in the gluteal region occurs after the first injection, which soon disappears. On the other hand, soon after the injection the odour of eucalyptol becomes perceptible in the expiratory air, due to the absorption of the preparation by the blood vessels and lymphatics. The great activity of this preparation is probably attributable to its absorption.

Morgenroth-Tugendreich, Berliner klinische Wochenschrift 1913, No. 26, p. 1207.

Berliner, Berliner klinische Wochenschrift 1913, No. 37, p. 1703.

Compare also Merck's Report 1910, p. 174.

The cases treated by the author included only a few cases in the initial stage, and the great majority were patients with extensive processes, not only those with simple dullness and catarrhal bruits in the apex, but also cases with extensive dullness, cavitation, tubercle bacilli in the sputum, febrile symptoms and rapid pulse. Even in the severest cases the injections displayed a remarkable antispasmodic and sedative action. Patients who were tortured by severe attacks of coughing and who derived no benefit from morphine, could usually give up the use of narcotics after a few injections. The alleviation of the cough resulted in an improvement in the night rest and in the general health. The appetite also improved and coincidentally there was an increase in weight. The night sweats disappeared within a short time, the expectoration became easier, the amount of sputum decreased, the sputum itself showed less pus and became more mucus-like. The tubercle bacilli disappeared in most cases, as did the bacterial flora of the mixed infection. In some tuberculous women who suffered from excessive vaginal discharge the latter also ceased within a very short time.

Berliner states that there is no special contra-indication to this treatment. The author has also used iodipin in the place of the oleum dericini*.

The above described method was investigated by Rosenfeld, Löwenstein and Silber. Rosenfeld confirms its usefulness; however, he occasionally observed abscesses and infiltrations, which induced him to administer menthol in dericin oil (12 p.c.) rectally. With this method he succeeded in obtaining quite satisfactory results in some fairly severe cases.

Löwenstein was able to confirm the beneficial action of Berliner's method of treatment in mild and in advanced cases. In his experience the simple technique makes it possible to carry out this treatment during the consulting hour. He lays stress upon the prompt action displayed by the injections on the distressing cough.

Silber observed that comparatively frequently the injection was followed by an embolic-like symptom accompanied by a brief sensation of chill; however, a few minutes after the occurrence of the phenomena the patients were calm and

* Compare the article on "Iodipin" in this Report.

Rosenfeld, Löwenstein, Silber, Berliner klinische Wochenschrift 1913, No 27, p. 1277.

could be discharged; the same observation was made by Berliner in one case. Silber also reports a case of tuberculous coxitis in which several deep fistulas discharged sanious pus; operation had already been refused as hopeless. Under this treatment the case improved within a short time to such an extent that a trial with this method appears indicated in suitable cases.

Eucalyptus Oil.

J. Elgart discusses Milne's treatment of scarlet fever*. His results differ from those of Koerber and Kretschmer, although he does not fully endorse Milne's views regarding the value of this method. As is well known, this treatment consists in lightly painting the patient's whole body, from the crown of the head to the toes, with eucalyptus oil, as soon as the diagnosis has been established. This application is repeated twice daily during the first four days, and then once daily on the subsequent six days. At the same time the tonsils are touched with 10 p. c. carbolic oil. In measles, after the appearance of the rash, the patient is similarly painted over with eucalyptus oil, and a muslin curtain moistened with eucalyptus oil is hung over the bed. This is done with the object of destroying the causal germs breathed out by the patient and to prevent their dispersion. A strip of muslin moistened with eucalyptus oil is hung round the throats of the other children in the same room, and their beds are sprayed from time to time with eucalyptus oil. According to Elgart, this method is an extremely useful prophylactic measure against scarlet fever and measles, and is particularly suited for closed institutions, boarding schools and children's hospitals. If a child which has been ill is allowed to return home, where the hygienic conditions leave much to be desired, there is always a danger of infection, although this occurs but seldom and may take place after other methods of treatment. However, according to Elgart, Milne's method diminishes the mortality in measles and scarlet fever, and the number of severe complications. However, he states that inhalations of lime water are equally effective, at least in

Elgart, Medizinische Klinik 1913, No. 31, p. 1251.

* Compare Merck's Report 1912, p. 190.

Koerber and Kretschmer, Merck's Report 1912, p. 191.

scarlet fever. He is, therefore, of opinion that a combination of both remedies should prove effective in combating scarlet fever.

Eulatin.

E. Hellmer, like other authors*, has prescribed eulatin in whooping-cough with satisfactory results. According to the child's age, he gave six to twelve tablets daily, and these were usually well borne, even in the presence of diminished gastric function. In several cases not only was expectoration facilitated, but coincidentally the vomiting was allayed or disappeared entirely. Usually, the author was able to dispense with the use of any other drugs, as under the influence of eulatin alone the malady ran a normal course. However, it is imperative to use the drug at the earliest possible moment. If the spasmodic attacks have already become very distressing, small doses of codeine or chloral hydrate may be given, which are said to increase considerably the action of eulatin. An important advantage of this drug is its freedom from any injurious action on the heart, and even in large doses it does not cause arrhythmia or intermittent pulse, as sometimes occurs with other remedies for whooping-cough. Nevertheless, in spite of the good action of eulatin hygienic measures must not be neglected.

The satisfactory results of eulatin treatment in whooping-cough induced Hellmer to try it in chronic bronchitis in adults, and in influenza associated with bronchitic manifestations. The results were uniformly satisfactory, inasmuch as the catarrhal symptoms improved and expectoration was facilitated.

Eumenol.

According to H. Ziemann experience has shown that women suffering from menstrual troubles experience considerably greater discomfort while residing in tropical countries than is the case at home, and these troubles may become extremely severe, although an objective examination may fail to reveal any definite reason. Since gynecological treatment in the tropics is often scarcely obtainable owing to the difficulty

* Compare Merck's Reports 1908—1912.

Hellmer, Zentralblatt für die gesamte Therapie 1913, No. 4, p. 171.
Ziemann, Archiv für Schiffs- und Tropenhygiene 1913, Vol. 17.

experienced in obtaining medical aid in many parts, the author draws the attention of medical practitioners in the tropics to eumenol, a preparation which he has found effective and which has already been discussed in my Annual Reports*.

The author usually prescribed one teaspoonful of eumenol thrice daily, to be taken shortly before the onset of the expected flow and for a few days after its appearance. In most cases he observed a marked diminution in the troubles, although sometimes there appeared to be a somewhat greater loss of blood. The remedy proved especially useful in neurotic dysmenorrhœa. In the tropics the use of eumenol tablets is particularly recommended since liquid eumenol has a bitter taste which is repugnant to many patients. The tablets, which are supplied sugar-coated, have the advantage of keeping better and are easier to stock; they can be swallowed whole. Two to four tablets are taken thrice daily. A course of treatment requires at least fifty tablets, in some cases one hundred tablets have to be taken to obtain a cure.

Euresol.

Euresol**, which has been recommended for the treatment of various diseases of the skin, such as acne, sycosis and seborrhœa, was used by W. Doering for psoriasis capitis in the form of a hair wash, as issued ready for use. The author found that this preparation apparently has several advantages over the customary remedies. He directs that the scalp be moistened with euresol hair tonic in the morning on getting up, and then rubbing it in with the fingers. It is not necessary to wash the scalp, as is the case with other remedies, and this has the advantage of not exposing the patient to the risk of catching a cold, as the scalp is dry by the time the toilet is completed. Since the spirit has a somewhat oily consistence it is not necessary to apply grease after this treatment. The application of euresol spirit is followed by the rapid disappearance of the itching and of the formation of scales***.

* Compare Merck's Reports 1899, p. 69; 1901, p. 80; 1910, p. 176; 1912, p. 193.

** Compare Merck's Reports 1898, 1899, 1905 and 1909.

Doering, Münchener medizinische Wochenschrift 1913, No. 6, p. 335.

*** For formulas for euresol hair wash see also Schweizer Wochenschrift für Chemie und Pharmazie 1913, No. 43, p. 649.

C. Schäfer was able to confirm this action in seborrhœa. The patients also stated that the growth of the hair was improved. Objective examination showed that the scalp assumed a healthier appearance and the scales had disappeared. If the scalp was dry the author directed the patients to apply a little olive oil to the hair. Euresol hair tonic proved ineffective in alopecia seborrhoica as far as replacing the lost hair was concerned, but it prevented the further loss of hair.

Eusitin.

Prophylaxis is, according to Hirschberg, an effective measure in obesity, and he is of opinion that the accumulation of fat might be effectively combated by limiting the ingestion of food to three meals a day. In order to combat the feeling of hunger occurring in the intervals between meals in carrying out this treatment he advocates the use of a preparation, so-called eusitin, which is per se not a food but consists of mucin substances. Its action depends upon mucilaginous substances extracted from the root of *Althæa rosea*, and its harmlessness was demonstrated by a large number of experiments undertaken by the author. These substances cause slowing of the gastric digestion and a marked decrease of the sensitiveness of the entire alimentary canal. For this purpose after every meal one eusitin tablet is allowed to dissolve slowly in the mouth, and should a feeling of hunger make itself felt in the intervals between meals, another tablet is taken. The tablets are intended to remove the disagreeable manifestations which accompany the feeling of hunger, such as headache, giddiness, etc. The feeling of hunger, too, is obtunded so that the patients gradually get accustomed to take only three meals daily.

Fibrolysin.

As during the past years, the contributions to medical literature published in 1913 demonstrate the great interest taken in this preparation by members of the medical profession. Its principal field of application is, as theretofore, to be found in those diseases in which the use of fibrolysin as a solvent

Schäfer, *Medico* 1913, No. 37.

Hirschberg, *Fortschritte der Medizin* 1913, No. 35, p. 970.

of cicatricial tissue is indicated. Thus J. Kayser reports some noteworthy successes following the use of fibrolysin in corneal cicatrices. It proved extremely useful as a clearing up agent particularly in leucoma consequent on corneal ulcer with hypopyon. After the ulcer had healed and as soon as the eye had lost its sensitiveness the author instilled one or two drops of fibrolysin thrice daily; in order to allay the pain which immediately follows the instillation the author applied cotton wool moistened with hot water. The result was all the more satisfactory the earlier the scar was treated. A combination of dionin and fibrolysin is also very useful. Kayser frequently first instilled one drop of dionin solution in order to render the tissue more receptive, and then applied fibrolysin a few minutes after the onset of chemosis. Another indication for fibrolysin in eye work is afforded by strictures of the nasal duct. Applied to the seat of the affection, according to Wolffberg, it rapidly displays its action so that after a few days the stricture becomes passable.

G. Werdnigg reports a case in which the external application of fibrolysin in the form of a plaster yielded an excellent cosmetic result. It was that of a woman with an unsightly scar on the neck left by an operation for goitre. Treatment consisted in applying a piece of fibrolysin plaster 2 cm. broad to the scar, renewing the application after a fortnight. After two months' treatment the scar was scarcely noticeable. The use of fibrolysin plaster proved equally satisfactory in the treatment of a scar caused by an operation for furuncle.

In cases of impermeable stricture of the urethra Lévy-Weissmann gave subcutaneous injections of fibrolysin and by this means the introduction of a sound was made possible after a short time. The treatment also led to an improvement in the patient's general health; the injections were painless and were well borne. Three or four subcutaneous injections usually proved sufficient, and the injection may be made in any

Kayser, *Wochenschrift für Therapie und Hygiene des Auges* 1913, Vol. 16, No. 26.

Wolffberg, *ibidem* 1913, Vol. 16, No. 44.

Werdnigg, *Klinisch-therapeutische Wochenschrift* 1913, No. 20, p. 607.

Lévy-Weissmann, *Journal d'urologie* 1913, No. 5.

part, not necessarily in the neighbourhood of the cicatricial tissue, as the drug acts irrespective of the site of injection.

M. Fraenkel reports the results obtained in the course of the past six years by the use of fibrolysin in the treatment of multiple sclerosis in Nonne's clinic. This method is simple and free from danger, for only rarely a slight rise of temperature (phenomena of anaphylaxis) occurs after the second or third injection, or later. The injections may be given for any length of time, and this is an advantage which is bound to exert a beneficial influence on the patient's mind in so chronic a nerve disease as multiple sclerosis, especially if the injections are made by the medical attendant himself. It is apparent from the author's statements that the customary measures adopted in the treatment of sclerosis, such as lukewarm baths, passive movements, gentle exercises, application of electricity, etc., assist the action of fibrolysin, hence institutional treatment is to be preferred to home treatment.

The value of fibrolysin in scleroderma is discussed by A. Sachnowskaja, T. Pawlow, L. Ehrlich, Moberg and A. B. Josefowitsch. In a number of cases Moberg has obtained an improvement by the use of large doses of fibrolysin. Sachnowskaja also observed alleviation of the pain after about ten injections of 1 to 2 c.c. On continuing this treatment the pains disappeared entirely and with the simultaneous use of baths and massage the skin became softer and more supple. On the other hand, Ehrlich records a case in which this treatment failed. Pawlow, too, doubts whether fibrolysin is useful in all cases, since scleroderma may improve under physical therapy alone without the use of other remedies.

The use of fibrolysin in pyloric stenosis is recommended by K. Petró, K. Lewenhagen and J. Thorling. They gave injections of fibrolysin in ulcer of the stomach and duodenum with signs of congestion with a view to preventing the

Fraenkel, *Neurologisches Zentralblatt* 1913, No. 1.

Sachnowskaja, *Wratschebnaja Gazeta* 1913, No. 11.

Pawlow, *ibidem*.

Ehrlich, *ibidem*.

Moberg, *Archiv für Dermatologie und Syphilis* 1913, Vol. 117, No. 4.

Josefowitsch, *Wratschebnaja Gazeta* 1913, No. 7.

Petró, Lewenhagen, Thorling, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie* 1913, Vol. 26, No. 2.

increase of connective tissue at the pylorus, as here the formation of scars may easily occur. As it is not easy to decide in every case whether a cicatricial stenosis is present, since congestion may be produced and persist for some time without this condition, the authors advise a trial with fibrolysin. Although the action of this drug cannot be accurately gauged since recourse is had to other remedial measures as well in the treatment of these symptoms, the authors feel justified in ascribing to fibrolysin a favourable influence which is borne out by their observations, particularly in one case in which during the four years following the first course of treatment with fibrolysin no marked retention took place in spite of three recurrences of the ulcer. In the authors' opinion fibrolysin treatment holds out less promise of success the more this retention in the course of time has developed into a cicatricial stenosis.

This finding is in keeping with other observations. For instance, S. C. Beck also points out that keloids or hypertrophic scars consequent on burns are influenced all the more quickly and favourably by fibrolysin the sooner the treatment is adopted. Although in quite recent cases massage may prove effective, in cases of long standing the simultaneous use of fibrolysin cannot be dispensed with. Its action, however, does not set in at once; in old standing keloidal scars often forty to fifty injections are required to effect the breaking down of the cicatricial tissue and produce so considerable a shrinking of the scar that it no longer projects above the normal skin. The injections may be made daily, but usually it is sufficient to give two or three injections a week, especially in children. For the site of injection the author selected the neighbourhood of the scar, and in sensitive patients the muscular tissue.

F. Watry obtained excellent results in two cases of maxillary periostitis. One case was that of a woman who in consequence of severe periostitis was unable to bring the incisors apart by more than 0.5 cm. Mechanical treatment led to an improvement but normal masticatory movement was not restored. A weekly injection of the contents of one ampoule of fibrolysin had an excellent effect on the masseter,

and masticatory movement became normal. In the other case a recurring ulcer had formed following the extraction of a wisdom tooth. As periostitis was also present several operations were performed whereby a scar had formed which occasionally suppurated. To soften the cicatricial tissue Watry injected every second day the contents of an ampoule of fibrolysin, giving altogether ten injections. Already on the eighth day a marked improvement set in, the movement of the joints became freer and less painful and the scar was softer to the touch. The masticatory movements became normal and an improvement in the general condition was also apparent.

Based on his experience K. W. Ipatow discusses the value of injections of fibrolysin in the treatment of arthritis deformans. He injected the preparation subcutaneously into the region of the shoulder and hips, and to assist its action prescribed baths, massage, exercises and mineral waters. His results led him to regard fibrolysin as a useful remedy in the treatment of arthritis. It allays or removes the pains and increases the mobility of the affected joints, although it does not effect a complete cure.

Brenner draws attention to the value of fibrolysin in chronic pneumonia, already alluded to by other authors*. In one case with two injections he obtained within a short time an improvement in the existing symptoms (the sounds at the edges of the dullness became clearer and the dullness at the middle lobe was diminished), and in the end complete recovery ensued without the slightest residue.

A paper by F. B. Counihan on the results of fibrolysin treatment in miner's phthisis is also of interest. As the morbid condition in this case is the result of a traumatic inflammation of the connective tissue leading to an extensive but not firm cicatrisation, the use of fibrolysin in miner's phthisis promises to be of some value. The author injected subcutaneously three times a week the contents of one ampoule, and he states that this dose should not be exceeded. Already after the third or fourth injection the general condition, the cough and expectoration showed an improvement, while sleep, appetite and ability to move about improved.

Ipatow, Wratschebnaja Gazeta 1912, No. 35—36.

Brenner, Münchener medizinische Wochenschrift 1913, No. 28, p. 1547.

* Compare Krusinger, Merck's Report 1908, p. 205.

Counihan, Transvaal Medical Journal 1913, No. 10.

Usually after five weeks the patients lost the cyanotic appearance of the face, respiration and talking became easier and in cases of moderate severity a cure may be expected within ten weeks. The author made the observation that at a certain stage during the treatment "colds" and pleuritic pains developed, and he attributes these manifestations to the fibrolysin displaying its maximum effect by leaving raw surfaces for infection and irritation in the lungs and pleuræ.

D. Berlin used fibrolysin as an adjuvant to the specific treatment of syphilis. As is well known, TOUTON already expressed the belief that combined treatment by fibrolysin and salvarsan marked an advance. His trials show that it is useful even in serologically very obstinate cases of syphilis (28.5 p.c.), if it is employed after an energetic specific treatment and then followed by another course of energetic specific treatment. On the other hand, he failed to observe any benefit if fibrolysin was used from the beginning simultaneously with the specific treatment.

A new method of using fibrolysin is proposed by A. H. TUBBY. As the excision of cicatricial tissue often fails to have the desired result even if followed by extensive skin grafting, he made a large number of incisions into the cicatricial tissue. The incisions are placed close together, not more than one-tenth of an inch apart; and great care is taken that they should penetrate not only into the subcutaneous fat, but also extend one-quarter or half an inch into the neighbouring healthy skin. No attempt is made to arrest the bleeding except by pressure, and when bleeding has ceased fibrolysin is vigorously rubbed in; and, if the scar tissue is very thick, a few drops are injected into the most prominent bands. In children, 0.9 c.c. (15 min.) and in adults 1.3 c.c. (20 min.) are injected. After this operation, the part is put up on a splint, in as much extension as possible, without tearing the soft parts, and is allowed to heal. This is accompanied by no excessive reaction and very little pain. After ten or fourteen days the wound will be healed, and the mobility of the part is very considerably increased. The operation is then repeated, and it rarely may be required three or four times. The results of this treatment are most

Berlin, Medizinische Klinik 1913, No. 27, p. 1081.

Tubby, British Medical Journal 1913, II, p. 1138 and II, p. 1203.

satisfactory; scars which have been tough and resistant become soft and supple, and the part regains its full mobility. The author recommends a similar method for the treatment of Dupuytren's contraction.

Of interest is a statement by N. Thiberge. In a child, aged $2\frac{1}{2}$ years, a laryngeal stenosis consequent on diphtheria and tracheotomy opposed the removal of the tube, but this difficulty was overcome by means of injections of fibrolysin.

Reports dealing with the use of fibrolysin in veterinary practice have been published by N. Kuzokon, H. Kriesche, J. Frucht, Schenkel, Bress and S. Miranda.

In the so-called posterior synechiæ consequent on iritis, inflammation of the ciliary body, ophthalmia, etc., in the beginning there is only adhesion of the iris to the capsule of the lens, but in time these adhesions are transformed into cicatricial tissue. Although the use of atropine, atropine and cocaine and physostigmine displays a curative effect on these adhesions, the drugs fail in the presence of more advanced scar formation, so that the animals suffer partial or entire loss of vision. In such cases Kuzokon has obtained successful results by first applying fibrolysin and then atropine. He achieved most satisfactory results in the cases reported with three to five injections of 11.5 c.c. of fibrolysin. The synechiæ either disappeared entirely or at least a marked improvement in vision took place. On the other hand, in the presence of catarrh fibrolysin is successful only in the first stage of the affection, when opaque tissue has formed on the surface of the capsule; however, even in these cases the author failed to observe a satisfactory result. Trials with the drug in parenchymatous keratitis yielded negative results.

A promising field of application for fibrolysin treatment is afforded by cases of thickening of the tendons and of the pastern joint, as in these other methods frequently fail

Thiberge, New Orleans Medical and Surgical Journal 1913, Vol. 66, p. 225.

Kuzokon, Veterinarny Wratsch 1913, No. 17.

Kriesche, Österreichische Wochenschrift für Tierheilkunde 1913, No. 14.

Frucht, ibidem 1913, No. 34.

Schenkel, Münchener tierärztliche Wochenschrift 1913, No. 34.

Bress, ibidem 1913, No. 33.

Miranda, Revista de terapeutica veterinaria, September 12, 1913.

and these affections cause considerable losses to owners of horses. The reports by Kriesche and Frucht show that fibrolysin is extremely useful, and in most cases a complete success is obtained after two to five injections. (Compare Merck's Report, 1912, page 203). Formation of scar tissue and thickening of the skin following superficial injuries is, according to Schenkel, made to disappear within a comparatively short time by fibrolysin.

Bress reports the case of a horse which in consequence of rubbing with oil of mustard exhibited necrosis of the skin of the side of the chest, and then a protuberance of skin as thick as two fingers developed. Two injections of fibrolysin made directly into the affected tissue led to the disappearance of the scar tissue. A similar case is reported by Miranda. It was that of a horse in which repeated application of cantharides ointment had produced an extensive swelling. In this case, too, the use of fibrolysin was followed by a speedy improvement and healing.

Fluoresceïn-Sodium.

Fluoresceïn-sodium, $C_{20}H_{10}O_5Na_2$, forms red pieces of a greenish lustre, or a red powder, which are soluble in water and alcohol, the solutions having an intense green fluorescence*. The latter is so pronounced that it is still plainly apparent in a solution containing one part in 2,000,000 parts. For this reason this preparation is a suitable indicator for testing the renal function, for which it has been proposed by H. Strauss. His method is as follows:

In the morning, after emptying the bladder, 1 gramme of fluoresceïn-sodium (uranin) is taken on an empty stomach in a cup of tea or cocoa. In healthy individuals the urine passed ten to twenty minutes later already exhibits a marked fluorescence, which it retains for about 35 to 40 hours. In the presence of disorder of the renal function the fluorescence makes its appearance later and lasts longer, and the diagnosis is based upon this fact. Since the fluorescence is much more easily discerned in an alkaline solution, it is advisable to add a little alkali to the urine to be tested as soon as fluorescence does not occur with sufficient clearness. Accord-

* Compare Merck's Report 1905, p. 81 and 1909, p. 211.

Strauss, Berliner klinische Wochenschrift 1913, No. 48, p. 2226.

ing to Strauss, the above mentioned dose usually* gives rise to a slight jaundiced appearance of the skin, especially if there is any difficulty in the elimination of the dye. On the other hand, the author never observed any unpleasant secondary effects. Cases in which the elimination lasts for 40 to 50 hours are classed by Strauss merely as suspicious. Persons in whom the elimination lasts longer than 50 hours also exhibited a delay in excreting the dye when phenol-sulphonephthalein was given*. Hence fluorescein-sodium may be regarded as a useful indicator for testing the renal function, all the more so since the internal administration of the preparation and the valuation of the fluorescence exhibited by the urine present no difficulties. If the method is employed in surgical diseases of the kidney with the use of ureteral catheterisation, according to Strauss, the difference between both kidneys at the beginning of the elimination of the dye is of greater importance than the difference at the end of the elimination, and it is advisable to extend the examination to about ten to thirty minutes following the introduction of the dye.

Folliculin.

Folliculin is the name given by J. Boas to a liquid extract prepared by exhausting senna pods with water; 1 gramme of this preparation represents the same amount of drug. The finished product is sterilized in closed bottles in order to render it stable. The extract issued in the form of tablets is said by the author to be less effective. The preparation is intended for use in habitual constipation in the place of infusion of senna pods. It is given in doses of one to three teaspoonfuls daily.

Boas, who has used folliculin for two years, states that it displays a prompt and reliable action, particularly in bedridden patients suffering from constipation. It is also indicated in the treatment of patients suffering temporarily from constipation, such as is the case with individuals who without suffering from severe chronic obstipation suffer from so-called sluggishness of the intestines, and when travelling or with an altered mode of living usually suffer from constipation.

* Compare the article on "Phenolsulphonephthalein" in this Report. Boas, *Therapie der Gegenwart* 1913, No. 1, p. 11.

Further, the author prescribed it with successful results in cases in which the strict observance of dietary and hygienic measures failed to achieve the desired result. In these cases one or two teaspoonfuls, in addition to suitable diet, suffice to produce a complete success, even if the most drastic purgatives have previously failed. Boas also used it with good results in several cases of inoperable cancer of the large intestine and rectum, in which the prevention of stagnation presents one of the most important therapeutic indications.

Like all laxatives folliculin also possesses the drawback that it loses its efficacy on prolonged use. In suitable cases somewhat larger doses may then be given. This extract of senna pods is free from injurious secondary effects.

Formaldehyde.

After Uspenski had demonstrated experimentally that formaldehyde is able to inhibit the growth of actinomyces even in dilute solution, N. Trinkler tried the use of formaldehyde in actinomycosis, and in the course of ten to fifteen years has made a careful study of its action. In his experience a mixture of 1 part of formaldehyde (40 p. c.) and 99 parts of glycerin yields the best results. At first he applied this mixture with a tampon to the wounds, but soon he proceeded also to inject the mixture into the indurations; he injected 10 to 15 c. c. in small portions into different places. According to the occurrence of a painful or inflammatory reaction the application was repeated daily or every second or third day. If fistulas were present 2 to 3 c. c. were also injected into these. The results obtained by this treatment, even in severe cases, show that formaldehyde is a very useful remedy in this affection.

H. Bourgeois gave interstitial injections of a mixture of equal parts of formaldehyde (40 p. c.), glycerin and alcohol (90 p. c.) in tuberculosis of the upper air passages. In a case of tuberculous ulcers on both sides of the fauces and palate he was able to demonstrate the value of this treatment by injecting formaldehyde into one ulcer only. Improvement set in and the proliferation disappeared almost entirely, whereas the untreated ulcer became worse. Only a few drops of the above

Uspenski-Trinkler, *Chirurgitscheskij Archiv Weljaminowa* 1912, Vol. 28, p. 729. — *Zentralblatt für Chirurgie* 1913, No. 13, p. 480. Bourgeois, *Progrès médical* 1912, No. 48.

mentioned mixture are injected, and the injections are made into different sites. When making the injection care must be taken to prevent the formaldehyde mixture from coming into contact with the mucous membrane. For cauterisation in laryngeal tuberculosis the author employed a mixture of 50 parts of formaldehyde (40 p.c.), 4 parts of glycerin, 10 parts of lactic acid and 20 parts of water. This mixture can also be used for cauterising granulations in chronic middle ear catarrh.

In several cases of empyema of the pleura G. Nyström tried repeated puncture followed by the injection of formalin-glycerin according to Murphy-Helling. For injection he used either 10 c.c. of a 4 p.c. formaldehyde-glycerin or 20 c.c. of a 2 p.c. formaldehyde-glycerin. In some cases this treatment led to a cure, but in most instances it failed. Therefore, in the author's opinion, it cannot be regarded as a substitute for thoracotomy, and it should be adopted only when an operation is apparently contraindicated.

According to a statement by A. Volkmar formaldehyde-sodium bisulphite* in the form of intravenous injections is said to prove very useful in gout. The author states that 5 c.c. of a 10 p.c. solution can be injected daily until the hepatic engorgement has disappeared. While Reichold confirms the successes reported by Volkmar, Königer advises a thorough clinical investigation of the method prior to its adoption in general practice. For this method of treatment a suitable preparation is issued under the name of "fonabisit"; it is supplied in ampoules of 5 c. c.**.

Formaldehyde-sulphurous acid, which is prepared by passing SO_2 into commercial formaldehyde, is said by Ph. Malvezin to be a useful reagent for detecting the presence of fuchsine in wine and in foodstuffs. Very dilute solutions of

Nyström, Hygiea, 1913, No. 9.

Volkmar-Reichold-Königer, Deutsche medizinische Wochenschrift 1913, No. 10, p. 486.

* Formaldehyde-sodium bisulphite, $\text{CHOH} + \text{NaHSO}_3 + \text{H}_2\text{O}$, according to K. Kraut forms colourless crystals which effloresce on exposure to the air. It is readily soluble in water and methyl alcohol, but only sparingly soluble in ethyl alcohol. (Liebig's Annalen der Pharmazie 1890, Vol. 258, p. 105.)

** Compare Vierteljahresschrift für praktische Pharmazie 1913, No. 3, p. 231.

Malvezin, Annales de chimie analytique 1913, Vol. 18, p. 193.

fuchsine, even if previously decolorized by animal charcoal or sulphurous acid, assume an intense violet coloration on the addition of this reagent. For instance, if wine is to be tested for fuchsine it is decolorized with not too much animal charcoal and filtered, 3 c.c. of the filtrate are shaken with 3 c.c. of the reagent. If necessary, the mixture is heated to boiling as this makes the test more sensitive. In the presence of fuchsine a violet coloration is produced, whereas other aniline dyes produce only a very faint flesh colour.

Formic Acid.

The assertion has been frequently made in the literature that the internal administration of formic acid in the form of sodium formate or in combination with alkaline fluids exerts a tonic effect on the muscles and removes the feeling of lassitude*. Amounts up to 4 grammes are stated to represent the daily dose, and are said to be borne without ill effects. As formic acid in a concentrated form has a caustic action it is evident that it can be given only in large amounts of liquid, and never per se. Dick drew attention to this fact some years ago, and stated that the highest harmless concentration was a 1 p.c. solution. Recently H. Eppinger reported a case of formic acid poisoning which shows that individual susceptibility may lead to the production of the secondary effects referable to formic acid, consisting in irritation of the kidneys and hæmaturia. In conjunction with his collaborators Eppinger took daily 3 to 4 grammes (45—60 grains) of sodium formate in order to study the conjugation of fatty acids with carbohydrates in the organism. Unfortunately the author does not state the concentration of the solution he employed, so that no conclusions can be drawn regarding the relationship of the solution to the toxic symptoms observed. Two persons tolerated the drug without any discomfort; in one person albuminuria and hæmaturia occurred which disappeared after five days. Since it may be assumed that the medication was carried out under the same conditions, as already stated, this result was undoubtedly due to an individual susceptibility to formic acid.

* Compare Merck's Reports 1903—1909.

Dick, Merck's Report 1909, p. 87.

Eppinger, Wiener klinische Rundschau 1913, No. 4, p. 49.

Eppinger's experiments on animals show that formic acid does not always undergo complete oxidation in the body. In these cases it is excreted by the kidneys and thus probably gives rise to the manifestations which were observed in the case cited above.

Galyl and Ludyl.

P. Troisfontaines describes two new preparations of arsenic, one of which he submitted to an exhaustive clinical investigation. The one, called "galyl", is tetraoxydiphosphaminodiarsenobenzol, the other, termed "ludyl", is phenyldisulphaminotetraoxydiaminodiarsenobenzol. Galyl contains 35.3 per cent., and ludyl 33 p. c. of arsenic. Both occur as light yellow powders, insoluble in water; they dissolve only on the addition of a little alkali.

Troisfontaines treated 21 cases of syphilis, which had not undergone any previous treatment, with galyl, which was injected in doses of 0.2 to 0.55 gramme (3—8 grains); the total amount injected was 1 to 1.9 grammes (15—28 grains). The small doses appear to produce the same effect as the large doses, and for this reason the author prefers on the whole the use of small doses. They cause the primary and secondary manifestations to disappear as rapidly as when the larger doses are employed. As secondary effects he frequently observed rise of temperature, headaches and digestive disturbances, vomiting and diarrhoea, these symptoms are, however, only transitory so that the author regards the preparation as being only slightly toxic. As regards efficacy he believes that it is equal to the other preparations of arsenic at present used in therapeutics. As a rule he combined treatment by galyl with an energetic course of mercurial treatment; however, in his experience the symptoms are cured usually just as quickly with galyl alone as with combined treatment. The action manifests itself in that the roseola usually becomes somewhat more pronounced a few hours after the injection, then blanches and disappears in the course of four or five days. The syphilides on the mucous membrane disappear with equal rapidity; on the other hand lenticular syphilides often fail to be influenced even at the third injection and disappear completely only after 18 to 20 days. In 50 p. c. of the cases treated

Troisfontaines observed the occurrence of Herxheimer's reaction. It usually follows the first injection, in some instances it also occurs after subsequent injections. The tertiary ulcerations healed in a normal manner; the author has not yet investigated the action of the drug in the secondary manifestations — iritis, alopecia, pigmented papules and astenia. He applied the Wassermann test in one case only, so that for the present nothing can be said on this point. Also the author's experiences with ludyl are as yet incomplete.

Gastrosan.

According to R. Schmidt-Wallberg, gastrosan* is an efficient remedy for the treatment of the most commonly occurring affections of the stomach and intestines. The author observed a rapid action in acute gastric and intestinal catarrhis, in which the use of the drug in combination with a suitable diet caused the disappearance of the vomiting and of the malodorous, often very watery stools. The diarrhoea ceased at the latest on the third day after the use of the remedy; the appetite improved as well as the general condition. The drug also proved useful in chronic diseases of the stomach and intestines, such as gastric dyspepsia and dyspeptic diarrhoeas, in which it caused the disappearance within a comparatively short time of the pressure in the stomach, the eructation and malodorous stools, even without the observance of a special diet. It also proved useful even in old-standing cases. Gastrosan displayed a surprising effect in hypersecretion, hyperæsthesia of the gastric mucous membrane, motor insufficiency of the stomach, and particularly in ulcer ventriculi. After taking the remedy the troubles were speedily alleviated, and on continuing this treatment the morbid changes disappeared. Thus a few slight cases of ulcer ventriculi in which the author administered gastrosan for several weeks subsequently remained free from symptoms. In severe cases this treatment had to be repeated, but it always succeeded in removing the troubles for a time.

Schmidt-Wallberg prescribed gastrosan tablets of 0.5 gramme ($7\frac{1}{2}$ grains), with instructions to let them disintegrate in water to facilitate their ingestion. He usually prescribed

Schmidt-Wallberg, Fortschritte der Medizin 1913, No. 36, p. 994.

* Compare Merck's Report 1909, p. 215.

one or two tablets to be taken three times a day, after meals, and in severe cases as much as three tablets three times daily. Neither large doses nor the continuous use of gastrosan for several weeks caused any unwelcome secondary effects.

Gelatin, Sterilized

Among the remedies at present in use to check bleeding gelatin occupies an important position. If all the authors who have up to the present reported on the use of gelatin* have been unable to acknowledge the great value of gelatin, or to achieve positive results, this is primarily due to the use of an unsuitable preparation, as has been recently confirmed by S. W. Muraschew, and also to the usually ineffective method of using gelatin. The above named author, following the example of other investigators, again draws attention to the fact that a reliable hæmostatic action can only be obtained when gelatin is introduced directly into the blood circulation, whereas the internal or external application of gelatin is of use only in special cases or as an adjuvant to its subcutaneous exhibition. If Muraschew demands that only a reliable form of sterilized gelatin, such as Merck's sterile gelatin solution, be used, he does so by reason of the numerous successes which have been obtained by its use and which afford the best proof of its careful preparation. This, however, requires considerable experience. If this is lacking an unsuitable preparation may easily be the result, and such occurrences are naturally designed to cast discredit on gelatin therapy. A case in point may be cited in illustration.

In the past year John reported that the investigations of Ciuffini had demonstrated the uselessness of gelatin as a hæmostatic, and this induced him to state that "Ciuffini's investigations have robbed gelatin treatment of much of its nimbus, as he was able to show that a sterilized solution of gelatin loses its action on the process of coagulation, and a 10 p. c. solution of gelatin administered by mouth or rectally causes no changes, or only very slight changes, in the blood coagulation."

* Compare Merck's Reports 1899—1912.

Muraschew, *Therapeutischeskoje Oboshrenie* 1912, No. 23.

John, *Münchener medizinische Wochenschrift* 1912, No. 4, p. 186.

Ciuffini, *il Policlinico* 1909, December, abstracted in the *Zentralblatt für innere Medizin* 1910, No. 48.

It is true that in his paper Ciuffini made a statement to the effect that "Non-sterilized gelatin increases very considerably the coagulation of blood; coagulation sets in more rapidly and in a short time becomes very marked. A gelatin solution which has been sterilized for half an hour at 130° to 135° C. in a steriliser loses its action on the process of coagulation". To this I would remark that the experiments conducted by Ciuffini are utterly worthless since he used a gelatin solution which had been heated to 130°—135° C. for half an hour. A gelatin of this description loses not only its property of solidifying but also most of the other properties possessed by gelatin. This does not prove that a properly sterilized gelatin solution is altered in the same way and that it becomes inefficient. In the case of Merck's sterile solution of gelatin from the beginning attention was drawn to the fact, and this has been repeatedly mentioned in my Annual Reports, that the solution of gelatin is so carefully sterilized that it differs only slightly from non-sterilized gelatin. With Merck's sterile solution of gelatin this careful sterilization is quite sufficient as it is not prepared from ordinary commercial gelatin, but with gelatin obtained from the cartilage and connective tissue of certified healthy animals, slaughtered under supervision of a veterinary surgeon. Its efficacy and advantages over inferior preparations made from commercial gelatin and supplied as "sterilized gelatin" are based upon this fact.

The insufficient action displayed by gelatin when administered orally is also most probably due to changes which the gelatin undergoes in the stomach and intestines prior to its absorption. For this reason H. Grau states that the effect of internal gelatin treatment is highly problematic. Nevertheless, the internal use of gelatin may occasionally be productive of good results if its administration is sufficiently prolonged. E. Ruediger reports the case of a patient whose blood clotted almost immediately on its withdrawal, so that the Wassermann test could not be applied. This was due to the fact that eighteen months before the patient had been advised by his medical attendant to take daily 40 grammes ($1\frac{1}{3}$ oz) of gelatin, and had continued this treatment, so that at the time of this observation he had consumed about 20 kilogrammes (44 lb.) of gelatin. Apart from the large doses,

Grau, Archiv für klinische Medizin 1911, Vol. 101, p. 150.

Ruediger, Medizinische Klinik 1913, No. 8, p. 293.

this case shows that the prolonged ingestion of gelatin has a certain prophylactic value.

Injected subcutaneously, the action of gelatin sets in somewhat quicker, but not always immediately. This observation has been confirmed in a large number of communications which have been mentioned in my Annual Reports. *Melæna neonatorum*, in which the hæmorrhages are ascribed to deficient power of coagulation of the blood, affords a special indication for gelatin injections. Further examples of this kind are reported by E. Lövegren. These afford a further confirmation of the statement mentioned above that subcutaneous injection of gelatin is the only permissible form of exhibition. The author treated ten cases of *melæna*. Five cases, all of which were treated with subcutaneous injections, recovered. On the other hand, among the cases in which gelatin was given by mouth or per rectum only one ran a favourable course. Hence the author recommends a trial with gelatin injections before proceeding to transfusion of blood, a method which has recently been proposed.

The action of gelatin injections on coagulation of the blood is confirmed by W. Schultze and K. Blühdorn. In some cases of pulmonary hæmorrhage Schultze observed that the time of coagulation of the blood was markedly shortened after an injection of gelatin. Blühdorn includes gelatin among the best hæmostatics. He advises making the injection always into the neighbourhood of the bleeding focus, and at the same time points out that gelatin injections are not always quite harmless and that occasionally they cause pain and fever. Therefore, caution is necessary, especially in pulmonary hæmorrhages, since the injections of gelatin may possibly exert an unfavourable influence on the fever. In the author's opinion the subcutaneous exhibition of gelatin may probably be assisted by its internal administration.

Mention may be made of a statement by A. Meyer who reports that plugging with a 10 p.c. gelatin solution proved useful in epistaxis. Merck's sterile gelatin solution is very suitable for this purpose.

Lövegren, Finska läkaresällskapets handlingar 1913, May. — Wiener klinische Wochenschrift 1913, No. 40, p. 1634.

Schultze, Münchener medizinische Wochenschrift 1913, No. 1, p. 4.

Blühdorn, Medizinische Klinik 1913, No. 11, p. 422.

Meyer, Zeitschrift für ärztliche Fortbildung 1912, No. 24, p. 751.

Glucose and Cane Sugar.

H. L ü t h j e again draws attention to the use of glucose in the form of enemata in diabetes mellitus. The method proposed by other authors was slightly modified by him in that he administered glucose by rectal injection, a drop at a time, by the proctoclysis method, of which he made extensive use in his clinic. He made the observation that most persons are able to absorb from the rectum daily one to two litres (35—70 oz) of a 5.4 p. c. solution of glucose [50 to 100 grammes], ($1\frac{2}{3}$ — $3\frac{1}{3}$ oz of glucose), and that the sugar absorbed is much better assimilated by diabetics than the sugar ingested per os. In order to ascertain whether the sugar administered rectally is converted prior to its absorption he undertook some experiments which showed beyond doubt that by means of glucose enemata the sugar content of the blood is increased. The better utilisation of glucose when applied rectally induces the author to advocate the use of rectal injections in suitable cases of diabetes. He also tried the intravenous injection of glucose; however, no conclusions can as yet be drawn from his results. Some insight into the action of intravenous injections of sugar is afforded by the investigations of S. J. T h a n n h a u s e r and H. P f i t z e r, who found that the injection of a 7 p. c. solution of glucose was without exception well borne. After the first injection of 20 grammes of glucose in normal individuals fractions of a gramme are excreted with the urine a quarter of an hour after the injection. The excretion of glucose in the urine on the administration of larger doses does not increase in proportion to the increase in the amount administered. In normal individuals the proportion of sugar in the blood sinks to normal a quarter of an hour after the injection of 500 c. c. of a 7 p. c. solution of glucose. Sufferers from hepatic affection exhibit hyperglycæmia without glycosuria for hours after the injection. In chronic nephritis with a high initial index a very steep curve is obtained with a return to the initial index after a quarter of an hour, with negligible glycosuria. In severe cases of diabetes mellitus the whole of the glucose injected is excreted with the urine, in slight cases only a small fraction is eliminated. Moreover, in severe cases the

Lüthje, Therapie der Gegenwart 1913, No. 5, p. 193.

Thannhauser-Pfitzer, Münchener medizinische Wochenschrift 1913, No. 39, p. 2155.

curve denoting the sugar content of the blood is not steep, but is flat and drawn out, and in slight cases closely resembles the normal values.

Experience must show whether the rectal injection of glucose is associated with risks. According to Rimbaud, caution is certainly advisable with children. In a child severely ill with scarlatinal nephritis the author injected rectally twice daily 350 c.c. of a 4 p.c. solution of milk sugar and also made two intramuscular injections of 50 c.c. of a 4.7 p.c. isotonic solution of glucose. An improvement in the renal function set in, but the general condition became worse, and the author believes that the meteorism and bilious vomiting were principally due to the enemata of sugar. In the author's opinion the meteorism caused cardiac weakness. These manifestations need not be feared if sugar is injected into the blood stream, as they are due to the rapid fermentation of the sugar in the intestine.

For the treatment of internal hæmorrhages a paper by E. Schreiber is of interest; he found that intravenous injections of glucose were effective in gastric and intestinal hæmorrhages. In a case of intestinal hæmorrhage in typhoid he injected 200 c.c. of a 20 p.c. solution on two consecutive days with the result that the bleeding was arrested by the third day. There was no rise in temperature nor the slightest elimination of sugar. Similar observations were made by the author in other patients. In a hæmophiliac with profuse menstruations he injected 200 c.c. of a 10 p.c. glucose solution and succeeded in arresting the bleeding, which otherwise lasted for at least eight days, within the course of three days. He believes that the hæmostatic action is due to the fact that, like hypertonic solutions of sodium chloride*, the concentrated solution of glucose produces hydræmia and attracts substances which promote coagulation. F. Kuhn came to an apparently opposite result. He was able to demonstrate experimentally that the property of causing coagulation of physiological saline solution is inhibited by the addition of glucose

Rimbaud, Gazette des hôpitaux 1912, No. 142. — Deutsche Medizinisch-Zeitung 1913, No. 15, p. 254.

Schreiber, Therapie der Gegenwart 1913, No. 5, p. 195.

* Compare von den Velden, Deutsche medizinische Wochenschrift 1909, No. 5, p. 197.

Kuhn, Deutsche Zeitschrift für Chirurgie 1913, Vol. 122, p. 90.

(4 p.c.). Experiments on animals led to the same results, for after the intravenous injection of glucose a marked retardation in coagulation occurred. The author draws the practical conclusion that glucose should be added to solutions intended for intravenous injection. This addition has in the first place a strengthening action and nutritive value, further an anti-coagulating and with it an anti-thrombotic effect. Hence glucose may be used for warding off thrombosis; in addition it raises the blood pressure and has an antitoxic action. According to Kuhn, an isotonic solution is obtained by adding 4 grammes of glucose to 100 c.c. of a 0.85 p.c. solution of sodium chloride. The dose for adults is 50 grammes ($1\frac{2}{3}$ oz) of glucose, and the maximum dose is 1 gramme per kilogramme body-weight. His standard prescription takes the form of Schücking's solution:

Glucose	4 grammes (60 grains)
Sodium saccharate	0.04 gramme ($\frac{2}{3}$ grain)
Calcium saccharate	0.04 „ ($\frac{2}{3}$ grain)
Sodium chloride	0.85 „ (12 grains)
Water	100 grammes ($3\frac{1}{3}$ oz)

Administered internally glucose is said to prove a good remedy for the after-effects of narcosis. E. Chauvin and M. Oeconomos ascribe the disturbances following operation or narcosis to acid intoxication, similar to that occurring in diabetic coma. These disturbances may be prevented by giving to the patient at night, on the day before the operation, 150 grammes (5 oz) of glucose in 300 grammes (10 oz) of water, with the addition of 0.5 gramme (8 min.) of tincture of nuxvomica and 3 grammes (50 min.) of tincture of cinnamon. Cane sugar, which has been recommended by several authors to stimulate the heart's action, should have the same action. Thus, Carter, *inter alia*, directed a 62-year-old woman to take with her meals at first 55 grammes (2 oz) and later 110 grammes (4 oz) of cane sugar to combat the myocardial degeneration present in convalescence from influenza, and the effect of this treatment shows that sugar acts practically as a specific in weakness of the cardiac muscle. In a case of uncompensated valvular defect H. Dingle had tried digitalis,

Chauvin-Oeconomos, *Bulletin général de thérapeutique* 1913; *Revue internationale de médecine* 1913, No. 2, p. 30.

Carter, *British Medical Journal* 1911, II, p. 1401.

Dingle, *ibidem* 1912, I, p. 66.

rest in bed and other remedies without success, but the œdema disappeared after the patient began to take 150 grammes (5 oz) daily of cane sugar for a month. St. E. Denyer often obtained remarkably good results by the use of sugar in primary cardiac weakness; on the other hand, he found it useless in the presence of œdema and pains due to angina pectoris or to disease of the kidney.

Cane sugar influences to a certain extent digestion by retarding the emptying of the gastric contents and thus submitting the food to a prolonged action of the peptic digestion. According to E. Thomsen the custom of taking a sweet course containing sugar after meals is justified, since it delays the onset of the feeling of hunger.

The fact that cane sugar is a trustworthy ecboic seems to have been forgotten. According to O. Piering, doses of 5 to 15 grammes (75 grains to $\frac{1}{2}$ oz) stimulate the functions of labour pains, if given every ten minutes in concentrated solution. Its usefulness is enhanced by the fact that, unlike other ecboics, it is non-toxic, and is readily taken. As it is said that childbirth is easy in women employed in sugar refineries, sugar may be found to be a prophylactic which, administered during pregnancy, may prove of use to pave the way for easy parturition. This is all the more possible since sugar is known to increase muscular strength and has a stimulant action.

Cane sugar and glucose possess in common a further property which is usually overlooked, i. e., an antiseptic effect which may be turned to account in the treatment of wounds. G. Magnus, Hoffmann, Barbo and Cocherel have drawn attention to this property. According to Magnus, sugar possesses disinfectant and antiputrefactive properties; it is capable of dissolving fibrin and thus effects a rapid cleansing of wounds, it stimulates secretion by influencing osmotic processes, acts as a deodorant and effects the formation of healthy granulations and rapid epithelization. It is an in-

Denyer, *Lancet* 1913, I, p. 1092.

Thomsen, *Zeitschrift für physiologische Chemie* 1913, Vol. 84, p. 425.

Piering, *Prager medizinische Wochenschrift* 1913, No. 3, p. 30.

Magnus, *Münchener medizinische Wochenschrift* 1913, No. 8, p. 406.

Hoffmann, *ibidem* 1913, No. 10, p. 568.

Barbo, *ibidem* 1913, No. 14, p. 792.

Cocherel, *Thèse de Paris* 1912.

nocuous, cheap remedy, and apparently for all practical purposes is per se sterile. Hoffmann confirms the statement that sugar exerts a very favourable influence especially on weeping, suppurating wounds with an abundant secretion. In his experience a mixture of equal parts of sugar and naphthalene is especially useful, which is used as a dusting powder. According to Barbo, Lücke already found that cane sugar per se (without the addition of iodoform or naphthalene) complies with the requirements made of a good wound dressing.

With the same object in view Cocherel used glucose as a dressing for wounds; it was applied either dry, or in some cases in 40—48 p.c. solution. If the dressing of dry glucose caused pain, the author administered morphine, or made use of a moist dressing of glucose.

The local application of cane sugar or of glucose deserves attention in gynaecological practice in the treatment of vaginitis and puerperal fever. According to F. Kuhn, the content of lactic acid in the vagina is lowered in pathological cases, and this plays a certain rôle in puerperal fever; the content of lactic acid, however, can be raised by the introduction of sugar (glucose or cane sugar). The sugar is converted into lactic acid, without the production of injurious side products. Moreover, lactic acid and unconverted sugar destroy or weaken pathogenic germs and exert a favourable action upon the mucous membranes of the vagina. Therefore, investigations should be undertaken with a view to ascertain whether the introduction of sugar into the upper genital passage after birth might not prove a valuable prophylactic measure against puerperal fever. Deposits of this nature might well be capable of flooding the genital passages with a solution of sugar and lactic acid for a few days and thereby prevent infections and alkaline decomposition.

For microscopic work G. Magnus advocates the use of concentrated solutions of sugar for preserving permanent preparations. For details of his method the original paper should be consulted.

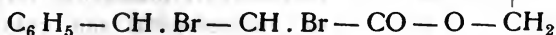
Lücke, *Ärztliche Mitteilungen aus Baden* 1883, No. 24, p. 212.

Kuhn, *Zeitschrift für Geburtshilfe und Gynäkologie* 1912, Vol. 70, No. 1.

Magnus, *Berliner klinische Wochenschrift* 1913, No. 14, p. 636.

Glycobrom.

Glycobrom is the glyceride of brominated cinnamic acid. It occurs as a white, amorphous powder containing about 50 p. c. of bromine. Melting point 66°—68° C. It has the chemical formula:



According to the pharmacological investigations of Béla von Issekutz glycobrom is decomposed in the animal organism and bromine ions pass into the blood, in addition practically indifferent substances are formed. After the administration of the drug the halogen content of the blood is altered in the same manner as following the ingestion of sodium bromide and sabromin. Whereas with the use of sodium bromide the toxic concentration of bromine in the blood is reached already after nine days, with glycobrom or with sabromin the complete therapeutic concentration is not even reached within the same time. Hence the dissociation of bromine from glycobrom takes place very slowly and therefore it is also more slowly absorbed. Hence the clinical study of this drug is indicated in those cases in which a slow and gradual saturation of the organism with bromine is aimed at, and only a faint bromine action is desired.

Glycogen.

Glycogen is a substance present in the liver and other organs, and also in blood and pus, which is usually obtained from fresh livers. It occurs as a white powder, to which is assigned the general formula $(\text{C}_6\text{H}_{10}\text{O}_5)_n$; however, it also contains water. Dried at 100° C. its composition is $6 \text{ C}_6\text{H}_{10}\text{O}_5, \text{H}_2\text{O}$. Glycogen is insoluble in alcohol; it is readily soluble in water to an opalescent, dextrogyrate solution. Dilute acids convert it into glucose.

According to Ghedini glycogen may be used in diseases of the liver to demonstrate that the function of the liver is more or less impaired. Normal liver contains a fer-

ment which converts glycogen into glucose, and in affections of the liver this ferment is said to disappear, or decrease. This ferment also passes from the liver into the blood, so that hepatic insufficiency may be diagnosed by demonstrating its presence in the blood, or by the quantitative estimation of the amount present in the blood. In applying this test a little blood is withdrawn from the cubital vein and clotted; 2 c. c. of the blood serum obtained are mixed with 10 c. c. of glycogen solution, which is prepared by dissolving 1.5 grammes of glycogen in 100 c. c. of physiological salt solution and adding two or three drops of solution of sodium hydroxide. The mixture is warmed in an incubator for half an hour at 37° C., whereupon double its volume of potassium thiocyanate is added, until it becomes clear. After filtering it is polarised in a 20 cm. tube. In the same way a blank test is prepared, using 2 c. c. of physiological salt solution in the place of the 2 c. c. of blood serum. If the rotation of the test containing serum is less than that of the blank test, this shows that a part of the glycogen has been converted into glucose and is a proof that the serum contains normal liver ferment. The less there is present the smaller is the amount of glycogen which has been converted and the smaller will be the difference between the serum test and the blank test. The decrease in the rotatory index of the mixture when glycogen has been converted into glucose is based upon the lower rotatory index of glucose. Glycogen: $\alpha_D = +196.6$ (Huppert); glucose: $\alpha_D = +48.3$ (Soxhlet). Ghedini states that this method yields good results and is worthy of further investigation.

Gold Chloride.

J. Jäger and M. Goldstein have found that a colloidal solution of gold causes a flocculent precipitate in the cerebrospinal fluid in certain pathological conditions. To apply this test they used the following reagent. 10 c. c. of a 1 p. c. solution of gold chloride are added to 1000 c. c. of freshly distilled water, and 10 c. c. of a 2 p. c. solution of potassium carbonate are added. The mixture is heated to boiling, and, shaking vigorously, 10 c. c. of a mixture of 1 part of formal-

dehyde solution (40 p. c.) and 100 parts of water are added. The solution of colloidal gold obtained by this means should have a deep purple colour, be clear and after standing for some time should not show any visible sediment.

In testing a specimen of cerebrospinal fluid the following procedure is adopted:

Fifteen test-tubes are taken and in the first 1.8 c. c. of 0.4 p. c. solution of sodium chloride are introduced, and into the remainder 1 c. c. is placed in each. To the first test-tube 0.2 c. c. of cerebrospinal fluid is added, and after mixing, 1 c. c. of the mixture is added to the second test-tube. Of the resulting mixture 1 c. c. is added to the third test-tube, and so on for each of the remaining test-tubes; in this way dilutions of the cerebrospinal fluid are obtained up to 1:100,000. To each test-tube 5 c. c. of gold solution are added as quickly as possible. At the same time a control test is made by mixing 1 c. c. of solution of sodium chloride with 5 c. c. of gold solution and this mixture should not change colour throughout the duration of the test, otherwise it is quite useless. After a few hours the test-tubes are examined for the presence of a possible flocculent precipitate. According to the authors, normal cerebrospinal fluid does not cause any flocculent precipitate; on the other hand, this is observed in the case of cerebrospinal fluid taken from paralytics, tabo-paralytics and syphilitics (cerebrospinal syphilis). Further, in one case each of tuberculous meningitis, cerebral abscess and epilepsy the authors observed a marked reaction; not, however, with other affections, such as neurasthenia, etc. They therefore regard the test as specific in paralysis and cerebrospinal syphilis.

Gold and Potassium Cyanide.

Gold and potassium cyanide occurs as a white crystalline powder, soluble in water; it has the chemical composition $\text{Au CN} \cdot \text{KCN} \cdot 2\text{H}_2\text{O}$.

After Chrestien and others had drawn attention to the therapeutic value of gold cyanide in scrofula and tuberculosis, Behring studied the bactericidal power of its water-soluble double salt, gold and potassium cyanide, and he found

Chrestien, Oesterlens Handbuch der Arzneimittellehre 1853, p. 147.
Behring, Gesammelte Abhandlungen zur ätiologischen Therapie der ansteckenden Krankheiten, Leipzig 1893. (Published by Thieme.)

that this compound is still capable of inhibiting the growth of anthrax bacilli in a dilution of almost 1:1,000,000. In the blood serum its bactericidal power is markedly diminished, to about 1:20,000—30,000, owing to the presence of albuminous substances; nevertheless, it is still considerable. However, H. Rittelmann casts doubt on the value of gold and potassium cyanide as an internal antiseptic in anthrax and infections due to typhoid and coli bacilli, since effective treatment in these cases would necessitate the use of doses displaying a toxic action.

Behring's observations were not made use of in therapeutics and indeed were scarcely noticed until recently C. Bruck and A. Glück undertook a clinical study of Merck's gold and potassium cyanide and their results awakened interest in medical circles.

The authors based their experiments upon the assumption that the introduction of gold and potassium cyanide into the blood stream in tuberculosis might be productive of a therapeutic effect inasmuch as the powerful bactericidal action of the compound should at least damage the tubercle bacilli, without seriously affecting the organism. Experiments on animals showed that this gold salt is not so extremely poisonous as its two principal components, gold and hydrocyanic acid, would lead one to assume. They also found that even a comparatively concentrated solution is not hæmolytic for human blood. To test its value the authors selected lupus, as chemotherapeutic treatment encounters particular difficulties in this disease, and therefore a beneficial influence on the affection would greatly enhance its value. Moreover, they avoided the use of any local treatment whatever in order to exclude any doubt regarding the action of gold and potassium cyanide. They adopted the following method:

The compound was always injected intravenously. For a full-grown, otherwise healthy individual it is advisable to begin with a dose of 0.03 gramme ($\frac{1}{2}$ grain) of gold and potassium cyanide, and after the third or fourth injection the dose is increased to 0.05 gramme ($\frac{3}{4}$ grain). For the present the use of larger doses should be avoided, although the authors

Rittelmann, Dissertation Stuttgart 1912. Berliner tierärztliche Wochenschrift 1913, No. 19, p. 349.

Bruck-Glück, Münchener medizinische Wochenschrift 1913, No. 2, p. 57.

have frequently given 0.08 gramme ($1\frac{1}{4}$ grains) without any permanent injury. In two cases they observed jaundice after the use of these large doses which rapidly disappeared, and this observation calls for careful watching of the liver and blood picture in prolonged gold treatment. A 1 p.c. stock solution of gold and potassium cyanide may be kept ready for use, and the doses required, i. e., 1 to 3 c. c. (= 0.01—0.03 gramme of gold and potassium cyanide), are withdrawn by means of a pipette and added to a freshly sterilized 0.6 p. c. solution of sodium chloride, made with freshly distilled water. 50 c. c. of solution of sodium chloride are used to dilute the 1 to 3 c. c. of the concentrated solution of gold and potassium cyanide, if larger doses of the latter are employed they are diluted with 100 c. c. The mixture is then preferably infused by the method first described by Weintraud (salvarsan infusion). It is advisable first to infuse a little solution of sodium chloride, and when it is apparent that injection is proceeding satisfactorily then the gold solution is injected, followed by the injection of a little solution of sodium chloride. The bleeding from the puncture is checked by holding up the arm and by pressure, whereupon the small wound is covered with a piece of adhesive plaster. If the injection is properly carried out it is quite painless; the occurrence of pain denotes that the injection fluid has penetrated into the tissue, in which case infiltrations may occur. If the injection is properly carried out the wall of the vein is not injured and remains permeable for the subsequent injections. The authors have so far given over 400 injections of gold and potassium cyanide and they state that a painful infiltration in the arm occurred only in one case, and disappeared completely within a few days. Usually, twelve injections were given in the course of four or five weeks. Injury to the kidneys was never met with. In many cases the injection is not followed by any general reaction, in some instances a very transient rise in temperature is noted, and more rarely vomiting and diarrhoea. The general health of the patients remained permanently unchanged. As is the case with tuberculin treatment, in numerous cases a local reaction occurred, which is regarded by the authors as a proof of the action of the compound, although it is not specific. In the majority of cases the therapeutic effect of the injections on the lupus processes is most marked. It is often very

soon manifest, already after the second or third injection. At first the colour changes, then the infiltrations subside. Ulcerated processes clean up, and epithelization sets in. This treatment proves least successful in the verrucose forms, and in the presence of wax-coloured, extremely caseous nodules situated in the centre of cicatricial foci.

The results obtained by Bruck and Glück show that by the use of infusions of gold and potassium cyanide alone without any other treatment something may be achieved. The preliminary trials undertaken by the authors with the combined use of infusions of gold and potassium cyanide and tuberculin promise even better results.

The use of injections of gold and potassium cyanide deserves full consideration in the treatment of syphilis. With about six injections, given in the course of twelve days, approximately the same effect was obtained in primary and secondary syphilis as is usually produced by a powerful preparation of mercury; the action of salvarsan, however, was not reached. On the other hand, the influence exerted on tertiary manifestations was only slightly inferior to that of salvarsan.

In an investigation of Bruck's method Bettmann found that the combined use of gold and potassium cyanide and old tuberculin in lupus yielded therapeutic results which were markedly superior to those produced by the use of the gold salt alone, although the effect of the latter is still worthy of note even if this method of treatment does not lead to a definite cure. In his experience the action of tuberculin is increased by the gold salt, and again stimulated in those cases in which it begins to fail. However, one must be prepared for a violent tuberculin reaction, which in cases of internal tuberculosis it is sought to avoid as much as possible. For this reason, in the author's opinion, objections may be raised against the use of the combined method on the very grounds upon which the greatest part of its efficacy most probably rests. These objections assume practical importance in the results observed by St. Pekanovich, although in this case the advanced stage of the morbid process must be taken into

Bettmann, Münchener medizinische Wochenschrift 1913, No. 15, p. 798.

Pekanovich, Deutsche medizinische Wochenschrift 1913, No. 28, p. 1355.

account in appraising the failures. The toxic action of the compound induced the author to try the first injections only in febrile patients who were severely ill. A surprising and violent reaction occurred which manifested itself principally by restlessness, respiratory embarrassment, hæmoptysis, in one case by hæmorrhagic stools and in another by vomiting and symptoms resembling collapse. In two patients who were seriously ill this treatment appears to have activated the tuberculous process and hastened the fatal termination.

Based on his experience L. Hauck considers gold and potassium cyanide to be a blood poison. He injected into a patient with an extensive lupous affection 0.34 gramme ($5\frac{2}{3}$ grains) within the course of 33 days (one dose of 0.02 gramme [$\frac{1}{3}$ grain], four doses of 0.03 gramme [$\frac{1}{2}$ grain] and five doses of 0.04 gramme [$\frac{2}{3}$ grain]). After an initial improvement symptoms of disintegration and ulcers occurred, followed by death. The post-mortem examination showed that death was due to poisoning, which the author ascribes to the gold salt*. Therefore, he is of opinion that the use of gold in the treatment of pulmonary tuberculosis is only permissible if caution is exercised, hence smaller doses than 0.02 gramme ($\frac{1}{3}$ grain) should be used at the commencement. Moreover, Junker has obtained good results by the use of small doses. At least he formed a good impression of the action of the drug in the treatment of uncomplicated pulmonary tuberculosis.

Since a rise in temperature was observed to follow the use of the doses employed by Bruck, and in Junker's experience febrile reactions should under all circumstances be avoided, he proceeded to use smaller doses which produced the same favourable effect, without apparently causing a febrile reaction. In pulmonary tuberculosis he advocates the use of 0.001 gramme ($\frac{1}{64}$ grain) for an initial dose. If this amount is borne without any febrile reaction the dose may be increased

Hauck, Münchener medizinische Wochenschrift 1913, No. 33, p. 1824.

* Bruck is of opinion that the case reported by Hauck is not one of gold cyanide poisoning; he maintains that it proves that in treatment with gold cyanide destruction of the red blood elements takes place. The fatal termination in the case described by Hauck might be due to several lethal causes. Therefore with regard to the dosage, great caution is required in debilitated persons or this treatment should not be adopted; in any case full attention should be paid to the blood picture.

Junker, Münchener medizinische Wochenschrift 1913, No. 25, p. 1376.

to 0.003—0.005 gramme ($\frac{1}{20}$ — $\frac{1}{12}$ grain); on no account should a dose of 0.02 gramme ($\frac{1}{3}$ grain) be exceeded. The injection can be repeated every third or fourth day.

In contradistinction to Pekanovich A. Mayer does not ascribe the toxic symptoms occurring during the use of gold and potassium cyanide to the cyanogen component of the drug, but, like Hauck, to its metallic components; this assumption coincides with Heubner's observations, who declares the gold salts to be capillary poisons. Further, among his patients Mayer never observed bleeding from the lung or intestines, nor any severe injuries whatever. On the other hand, doses of 0.01 to 0.03 gramme ($\frac{1}{6}$ — $\frac{1}{2}$ grain), injected intravenously, were not given in such dilute solutions as advocated by Glück, Bettmann and Junker. He believes that, apart from a possible "water-error", a stronger concentration is more effective and less dangerous. In his opinion a combination of gold and potassium cyanide with choline should prove particularly useful.

A further investigation of Bruck's method in lupus was undertaken by A. Ruete. It is true he was able to observe a slight improvement in several cases, but did not succeed in obtaining a cure. The author also treated two cases of lupus erythematosus with gold and potassium cyanide and tuberculin. In one, a case of long standing, neither a cure nor an improvement resulted; in the other case, an acute form in which no deeper infiltrations were present but only redness and slight formation of scales, a cure was obtained after seven injections of gold and potassium cyanide. The author ascribes the cure to the gold salt, in particular to its property of influencing the capillary system.

A very favourable opinion of the value of gold and potassium cyanide in the treatment of lupus is expressed by K. Walter, F. Poór and G. B. dalla Favera, whereas A. Pasini was unable to observe any uniform action on tuberculous processes of the skin. Like Ruete he was only able to obtain an improvement, but no definite cure. In his ex-

Mayer, Deutsche medizinische Wochenschrift 1913, No. 35, p. 1679.

Ruete, Deutsche medizinische Wochenschrift 1913, No. 36, p. 1727.

Walter, Przegląd Lekarski 1913, No. 32.

Poór, Gyogyaszat 1913, No. 39, p. 658.

Favera, Giornale italiano delle malattie veneree e della pelle 1913, No. 4.

Pasini, *ibid.*

perience the gold salt is incapable of destroying the causal agent of the disease, but this does not hinder it from being often useful on account of its property of stimulating epithelization and scar formation.

In his latest publication Bruck again deals with the chemotherapy of tuberculosis. He considers the selective influence of gold cyanide on tuberculous foci to be beyond doubt. It is as yet not established whether this effect is displayed primarily on the causal agent or on the anatomical substratum, and also whether gold cyanide treatment in its present form can already claim practical importance. However, since an efficient compound is available steps should be taken to improve it. For some months the author has investigated, *inter alia*, a combination of gold cyanide and choline prepared by me, but up to the present without any noteworthy successes.

F. von Poór is of opinion that gold and potassium cyanide is not yet fitted for use in general practice, but he recommends it for clinical use, since its intravenous injection undoubtedly displays a favourable influence on tuberculosis of the skin, especially in lupus vulgaris. He did not observe any toxic symptoms among his patients. He injected doses of 0.05 gramme ($\frac{3}{4}$ grain), and in those cases in which prolonged treatment was possible he allowed an interval of two or three weeks after the first twelve or thirteen injections, followed by a further series of ten or twelve injections. By this means the compound was used for a prolonged period. Especially in extensive lupus this treatment produced a rapid improvement, which was otherwise not obtainable in such severe cases either by the use of tuberculin or by the internal or subcutaneous use of any other remedy, coupled with indifferent external treatment. As he confined his investigations to the action of gold and potassium cyanide on tuberculous affections of the skin, he employed the compound only in those cases in which no internal organs were affected, such as the heart, lungs and kidneys.

J. Grünberg undertook trials with Bruck's method in syphilis. On the whole he used the same doses as suggested by Bruck, with this difference that he began with a dose of

Bruck, Medizinische Klinik 1913, No. 46, p. 1881.

Poór, Deutsche medizinische Wochenschrift 1913, No. 47, p. 2304.

Grünberg, Therapeutischeskoje Oboshrenie 1913, No. 9.

0.01 gramme ($\frac{1}{6}$ grain). The injections were made every third or fourth day. The results obtained in four cases, according to Grünberg, show that gold and potassium cyanide is a preparation which undoubtedly exerts a favourable influence on the syphilitic manifestations in all three stages, whereby the primary affections and the gummata react most markedly. The author considers further trials with the drug to be advisable, all the more so since it is borne without reaction, apart from slight intestinal disturbances. On the other hand, G. Burzi, who used the drug in syphilis and in some cases of skin disease, does not share the view that it is quite harmless.

With regard to the mode of action of gold and potassium cyanide the works of W. Heubner and A. Feldt should be consulted.

The action of intravenous injections of gold and potassium cyanide and other compounds of gold on mouse cancer has been studied by C. Lewin. The injections are followed by excessive hæmorrhage in the tumour, and this effect is most probably due to the action of gold salts of poisoning the capillaries, already demonstrated by Heubner. The nourishment of the tumour is thereby inhibited, or the supply of blood to the tumour becomes insufficient for the same reason, whereby the gold compounds are retained in the tumour in considerable amounts, with the above mentioned result. Finally the tumour is to a great extent changed into a necrotic mass.

Hediosit.

The value of hediosit* in diabetes is discussed by O. Gaupp. According to his observations this remedy reduces the elimination of sugar, but does not influence the acidosis. In contradistinction to the experience of Strauss and other authors he never observed diarrhœa after the administration of this drug. In four cases hediosit was given so as to permit a comparison between the elimination of sugar with standard diet alone, on the one hand, and on the other with standard

Burzi, *Riforma medica*, October 11, 1913.

Heubner, *Münchener medizinische Wochenschrift* 1913, No. 7, p. 357
and *Deutsche medizinische Wochenschrift* 1913, No. 15, p. 690.

Feldt, *Deutsche medizinische Wochenschrift* 1913, No. 12, p. 549.

Lewin, *Berliner klinische Wochenschrift* 1913, No. 12, p. 541.

* Compare Merck's Report 1912, p. 211.

Gaupp, *Medizinische Klinik* 1913, No. 26, p. 1040.

diet + 30 grammes (1 oz) of hediosit, further with standard diet + 100 grammes of bread ($3\frac{1}{3}$ oz) and lastly with standard diet + 100 grammes ($3\frac{1}{3}$ oz) of bread + 30 grammes (1 oz) of hediosit. In one case in which on a vegetable day 30 grammes of sugar were excreted, with the simultaneous use of hediosit the amount of sugar fell to 8 grammes on the next vegetable day. In another case the sugar excreted amounted to 31.25 grammes with standard diet, and to 45 grammes with standard diet + 100 grammes of bread, while with standard diet + 100 grammes of bread + 30 grammes of hediosit it amounted to only 19 grammes. The action of hediosit was most manifest on the vegetable days.

Hedonal.

Since the publication of my last report* on hedonal anæsthesia the following papers have appeared dealing with this subject:

C. M. Page states that the intravenous infusion of hedonal is a valuable method in suitable cases, and the possibility of an overdose constitutes the only danger. He used for infusion a 0.75 p.c. solution in physiological salt solution, warmed to 40° C., of which 50 to 150 c.c. were continuously infused into the saphenous vein. As a rule, deep anæsthesia set in after from five to ten minutes, associated with muscular relaxation, whereby the pulse and respiration remained good and only the blood pressure showed a slight fall. Occasionally a mild stage of excitement occurred. Great importance attaches to infusing the solution of hedonal at the proper rate. If it is infused too slowly the onset of anæsthesia will be usually delayed; on the other hand, too rapid infusion may lead to cyanosis. As a rule the anæsthetic stage is followed by sleep lasting for several hours, as much as twelve hours. This method has the advantage that pulmonary complications are very rare, also post-operative headache or vomiting occur only in a very few cases. An overdose may cause respiratory depression and in consequence of the falling back of the

* Compare Merck's Report 1911, p. 260.

Page, Mennell, Sargent, Silk, Corner, Dobson and Ward, Medical Society of London, October 28, 1912. — *Lancet* 1912, I, p. 1258. — *Klinisch-therapeutische Wochenschrift* 1913, No. 2, p. 70. — *Wiener klinische Rundschau* 1913, No. 32, p. 509. — *Medizinische Klinik* 1912, No. 39, p. 1596.

tongue the respiration may be obstructed, and herein lies the danger. The author states that hedonal anæsthesia is principally indicated in operations on the head and throat, and also in abdominal operations. Hence it is indicated in cases of goitre, phlegmons of the throat, and operations on the brain and spinal cord, particularly in those cases which are likely to be followed by prolonged after-pain. Thus Mennell and Sargent have obtained very satisfactory results in operations on the brain. Silk and Corner also express a very favourable opinion of hedonal anæsthesia. On the other hand, Dobson states that the mortality with hedonal anæsthesia is greater than with other methods of inducing anæsthesia, and he attributes this to the greater risk of pulmonary complications supervening.

Barrington Ward tried hedonal anæsthesia in a large number of children, for which it is said to be particularly suited. However, the difficulty lies in selecting a suitable vein for the infusion. 30 to 680 c.c. of hedonal solution are required to produce a satisfactory degree of anæsthesia. Ward states that the skin reflexes are not abolished, since there is only a slight margin between their abolition and the occurrence of a dangerous depression. Once anæsthesia has been induced only small amounts are required to maintain it. Among seventy cases the author had only one death, and in the case of this child status lymphaticus was present, which would have caused difficulties even with the use of other methods of anæsthesia.

G. A. H. Barton also reports a case of death under hedonal anæsthesia. He had infused 500 c.c. of hedonal solution within five minutes into an ill-nourished patient when the operation was commenced — opening and draining both frontal sinuses. The operation lasted $1\frac{1}{2}$ hours and 1000 c.c. were infused in all.

N. J. Beresnegowski, who has collected a vast amount of experimental and clinical experience regarding hedonal an-

Barrington Ward, *British Journal of Children's Diseases* 1913, Vol. 10, p. 17.

Barton, *Royal Society of Medicine, Section of Anæsthetics*, November 1, 1912. — *British Medical Journal* 1912, II, p. 1311.

Beresnegowski, *Chirurgitscheski Archiv Weljaminowa* 1913, Vol. 29, p. 208. — *Zentralblatt für die gesamte Chirurgie und ihre Grenzgebiete* 1913, Vol. 2, p. 404.

æsthesia, ascribes the cases of death after hedonal anæsthesia to the after-effects displayed by hedonal on the respiratory centre, kidneys and heart. In his opinion hedonal occupies a place in the middle between ether and chloroform. According to his pharmacological investigations the cardiac action becomes increasingly weaker in proportion to the amount of hedonal introduced, and also the blood pressure falls in the same ratio. He was also able to demonstrate that hedonal causes changes in the lungs, whereby the picture of pulmonary œdema preponderates. In order to avoid the risk of thrombosis he adopted Fedoroff's suggestion of making the intravenous infusions peripherally, but he came to the conclusion that this measure does not obviate this danger. He saw thrombosis in nine cases out of forty-five.

On the other hand, Saidman, Rydник and Kammer express a very favourable opinion of the value of hedonal anæsthesia. According to their statements cardiac disturbances and irritation of the kidneys are not to be feared, and there is a wide margin between the toxic and the anæsthetic dose of hedonal. Further, hedonal excites the nerves in a far slighter degree than ether or chloroform. Therefore, in opposition to other authors Kammer considers that hedonal anæsthesia is not contra-indicated in the presence of heart disease, arteriosclerosis or affections of the kidneys. He employed hedonal anæsthesia in 106 operations, and the two cases of death were not, in his opinion, due to the anæsthesia.

Hegonon.

The best results are obtained with this silver-albumin* preparation, according to E. Rosenfeld, in quite recent cases of gonorrhœa. Of 28 cases he succeeded in curing 14 in the course of three days by abortive treatment, without employing a solution of greater concentration than 0.25 p.c. Treatment with hegnon also yields satisfactory results in incipient gonorrhœa in the anterior urethra, if four to six injections are made daily. If complications are already present, such as

Saidman, Zentralblatt für Chirurgie 1913, No. 24, p. 970.

Rydник, Russkij Wratsch 1912, No. 6.

Kammer, Deutsche medizinische Wochenschrift 1913, No. 44, p. 2170.

* Compare Merck's Reports 1910 and 1912.

Rosenfeld, Deutsche medizinische Wochenschrift 1913, No. 41.

acute and subacute epididymitis, prostatitis, spermatoecystitis and folliculitis, or if there are infected para-urethral passages or soft infiltrations of the anterior urethra, a special preparatory treatment in addition to injections of hegonon is indicated, for which purpose the author prefers the use of gonococcal vaccine. In very old cases dilatation of the urethra could not be dispensed with. The occurrence of fresh complications during treatment with hegonon was not observed. Rosenfeld lays stress upon the freedom from irritant action of hegonon. In his opinion the greater the freedom from irritant action of an antigonorrhœic, to be injected in acute anterior urethritis, the greater is the certainty with which the reflex associated movements of the posterior urethra, bladder and adnexa can be prevented.

L. Weiss also found that hegonon is free from irritant action. In his experience a 3 p. c. solution is best suited for abortive treatment. This is injected on three to five consecutive days and retained for four minutes. As a rule, the gonococci have disappeared by the second or third day; should this treatment fail the customary treatment with Janet's injections may be continued without apprehension, and by this means the morbid process is often shortened. The author shares Rosenfeld's view that the best results are obtained in cases in which the gonococci have not penetrated into the cells in any large amounts.

For injection F. Antoni employed a 1—2:300 solution of hegonon, and for irrigation under pressure solutions of 1:500—2000.

Hexamethylenetetramine. (Amphotropin, Cystopurin, Hetralin, Hexal, Urotropine.)

The action of hexamethylenetetramine in affections of the urinary passages is due, as is well-known, to the powerful antiseptic properties of the formaldehyde* liberated within the organism. It is therefore of interest to establish whether this decomposition product of the drug is present in the urine, as this might assist in elucidating the reason of its failure to display

Weiss, *Archiv für Dermatologie und Syphilis* 1912, May. Vol. 113.
Antoni, *Hygiea* 1912, May.

* Compare also Brinkmann, *Norsk Magazin for Laegevidenskaben* 1913, No. 10, *Deutsche medizinische Wochenschrift* 1913, No. 47, p. 2314.

a therapeutic effect. The investigations of Cabot and L'Esperance showed that after the use of urotropine the presence of formaldehyde could be demonstrated only in about 50 p. c. of the patients, and in the patients who gave no reaction the presence of formaldehyde could not be demonstrated in the urine even on increasing the doses. To demonstrate the presence of formaldehyde in the urine the authors adopted Burnam's test*, which was applied as follows: To 10 c. c. of recently passed urine are added 3 drops of 0.5 p. c. solution of phenylhydrazine hydrochloride and 3 drops of 5 p. c. solution of sodium nitroprusside, and a few drops of concentrated solution of sodium hydroxide are poured down the side of the test-tube. If formaldehyde is present, a purple colour is produced, which rapidly changes to dark green and then gradually to yellow. If no formaldehyde is present, a reddish coloration is produced, which slowly changes to yellow.

Occasionally it is of interest to demonstrate the presence of formaldehyde, or of urotropine, in the cerebrospinal fluid, for instance, in the differential diagnosis of hydrocephalus. W. Usener studied the cerebrospinal fluid in pathological conditions, and he found that after the use of urotropine in serous meningitis and hydrocephalus it showed a normal concentration, hence in these diseases there is apparently no disturbance of secretion, whereas in tuberculous meningitis a decrease in the amount of urotropine passing into the fluid could be demonstrated.

H. Triboulet and F. Lévy advocate the subcutaneous use of urotropine in the treatment of typhoid, and also in infectious enteritis and in septicæmia. At first the authors injected twice daily 0.4 gramme (6 grains), and increased the daily dose up to 6 grammes (90 grains). With this treatment they succeeded in three cases in causing the disappearance of the diarrhoea and an abatement of the fever, which never lasted for longer than three weeks. At the same time a benign albuminuria made its appearance, and transient pain and tenesmus

Cabot-L'Esperance, Boston Medical and Surgical Journal 1912, Vol. 167, No. 17, p. 577.

* Compare Merck's Reagenzien-Verzeichnis 1913, p. 54.

Usener, Zeitschrift für Kinderheilkunde 1913, No. 2, p. 111.

Triboulet-Lévy, Presse médicale 1913, No. 16, p. 145.

on passing urine, which the authors ascribe to an irritant by-effect of urotropine on the bladder.

A paper by A. Leibecke on the secretion of urotropine by mucous membranes and serous membranes deserves special mention in connexion with the use of this drug. The author came to the following conclusions: Urotropine is excreted in the urine after about 15 minutes, in the cerebrospinal fluid after about 45 minutes, in the milk after about one hour, in pus from the ears and bronchi after about two hours, and in peritoneal pus certainly within four hours. It disappears from the pus from the ears after fifteen hours, from the bronchial pus after thirty hours, from the milk after twenty-one, and from the cerebrospinal fluid after fifty-three or seventy-seven hours. The highest concentration in the milk and cerebrospinal fluid is reached almost in the first moment of its appearance in these fluids; in the pus from the ears only after four to six hours, and the same probably holds good also for the bronchial pus. With the same dose, i. e., 0.25—1 gramme, the highest concentration observed in the pus from the ears and bronchi exceeded 1:10 000, in the cerebrospinal fluid it amounted to from 1:12 to 1:15 000, and in bronchial pus to about 1:20 000. The lowest concentration is found in milk. The concentration of urotropine in the cerebrospinal fluid and in the pus from the ears in children, after doses of 0.25—1.5 grammes, is quantitatively by no means proportional to the amount of the dose, nor is it in strict relation to the weight of the patient. There is no accumulation of urotropine either in the milk, in the cerebrospinal fluid or in the pus from the ears. Therefore, for therapeutic trials it is advisable to give larger doses at intervals of six or seven hours. In view of the fact that a concentration of 1:10 000 to at most 1:6 000 in the pus from the ears may be obtained, there is a possibility that it may display an antiseptic action, although this has not been proved. The customary therapeutic doses may exert an injurious influence on the kidneys, but this may in all probability be avoided by taking large amounts of fluids.

In succession to the above report mention may be made of a publication by Zimmermann, who believes that the use

of urotropine may prove beneficial in the treatment and prophylaxis of otogenous meningitis. He believes that the amounts excreted in the brain after the internal or subcutaneous exhibition of the drug are capable of displaying a bactericidal action. Of special importance is the fact that this effect can be obtained already by the use of harmless doses. The author seeks to explain the effect of urotropine by assuming that it acts in the same way as in the urinary passages, i. e., its action is based upon the liberation of formaldehyde. However, he never succeeded in demonstrating the presence of formaldehyde in the cerebrospinal fluid, a fact which is in opposition to the findings of other observers. Nevertheless, he advocates the use of urotropine in suitable doses in cases in which inflammatory processes are at work in the vicinity of the dura, primarily as a prophylactic measure (1.5 to 2 grammes [24 to 30 grains] daily), and recommends a trial even when meningitis is established.

A paper by Suzuki deals with the antiseptic action of urotropine in the urine. According to his investigations the growth of pus organisms in the urine is inhibited after seven days by a daily dose of 1.5 grammes (24 grains) of urotropine, and of *Bacillus pyocyaneus* after eight days. If daily doses of 2 grammes (30 grains) are given, the growth of staphylococci is inhibited already on the fourth day, and of *Bacillus pyocyaneus* on the sixth day, while the excitors of fermentation cease to grow already on the second day.

W. Cuntz also confirms the view that hexamethylenetetramine (urotropine) is a very useful drug for combating bacterial inflammations and catarrhs of the urinary passages. However, he states that in isolated cases the use of preparations of hexamethylenetetramine may aggravate the existing symptoms. Even with the customary dosage and when taken in water after meals, irritation of the excretory urinary passages may supervene, which manifests itself by albuminuria or hæmaturia. Hence hexamethylenetetramine and urotropine cannot be regarded as harmless and should not be prescribed as a matter of routine, but rather the patient should be kept under observation and his urine examined. If the drug is not tolerated

Suzuki, *Mitteilungen der medizinischen Gesellschaft Tokio* 1912, Vol. 26, No. 8.

Cuntz, *Münchener medizinische Wochenschrift* 1913, No. 30, p. 1656.

unwelcome sequelæ can be avoided by immediately suspending its use.

In the treatment of pyuria and bacteriuria A. R. Jordan lays stress upon the estimation of the acidity of the urine by means of exact titrimetric methods. To increase the acidity he usually prescribed urotropine, which he found very useful.

According to A. C. Burnham, hexamethylenetetramine is very useful in surgical cases, in which it can be given in daily doses of 12 to 18 grammes (180—270 grains) (!), if no idiosyncrasy to the drug is present. The occurrence of hæmaturia may be prevented by the plentiful supply of alkalis. Hexamethylenetetramine is useful as a prophylactic particularly in more extensive as well as minor procedures, such as cystoscopy and catheterisation of the ureter. La Roque also advocates the use of larger doses than have been given hitherto (4 to 8 grammes [60—120 grains] daily). In his experience it is a good prophylactic and curative agent in gastric paresis consequent upon abdominal operations, when the formation of gas is above normal. Further, the use of urotropine, in addition to other measures, is indicated in biliary infections, colitis, duodenitis and ulcus ad pylorum. The author is of opinion that a single large doses is more effective than the prolonged use of small doses, and he states that the irritation of the bladder and the hæmaturia which occur after the use of large doses are not dangerous and disappear of their own account as soon as the use of the drug is discontinued.

Hexal*. The use of hexamethylenetetramine sulphosalicylate is discussed by E. Bäumer, G. Fritsch, O. A. Kowanitz, R. Boer, Schömann and E. Schwarz.

Kowanitz used the drug in a large number of cases of chronic cystitis and retention of urine due to hypertrophy of

Jordan, Journal of Clinical Researches 1913, Vol. 6, p. 90.

Burnham, Medical Record 1913, Vol. 84, p. 15.

la Roque, Therapeutic Gazette (Detroit), July 15, 1913.

* Compare Merck's Report 1912, p. 222.

Bäumer, Berliner klinische Wochenschrift 1913, No. 28, p. 1308.

Fritsch, Deutsche medizinische Wochenschrift 1913, No. 28, p. 1370.

Kowanitz, Wiener klinische Wochenschrift 1913, No. 1, p. 19.

Boer, Dermatologisches Zentralblatt 1913, No. 5.

Schömann, Riedel-Archiv 1913, No. 3, p. 35.

Schwarz, Riedel-Archiv 1913, No. 9, p. 1.

the prostate, and he found that it caused increased diuresis, and that it converted the alkaline reaction of the urine into an acid one, while the urine soon became clear. In addition it displays a sedative effect. In his experience three doses of 1 gramme (15 grains) a day are sufficient, and these cause no undesirable secondary effects. Fritsch was unable to confirm the diuretic effect of the drug; however, he speaks very favourably of its sedative action. He also made trials with the combined use of yoghourt and hexal with a view to obtaining a favourable influence on digestion and thereby increase the action of the drug. He made the important observation that even in non-clinical forms without a special diet this combination of hexal and yoghourt was able to display an extremely satisfactory sedative effect on the function of the bladder. It manifests itself in the cessation of the troublesome strangury and in a marked increase of the impulse of the will on the muscular apparatus of the bladder. After the use of the drug for several weeks (0.5 gramme [$7\frac{1}{2}$ grains] thrice daily) the incontinence was removed and the times for daily micturition could be selected at will. Hexal is also capable of exerting a favourable influence in cases of already established senile incontinence.

Hexal is also very useful in urethritis gonorrhoeica posterior and gonorrhoeal urethrocystitis, as it appears from the reports by Bäumer, Schwarz and Boer. According to Schömann it is also useful in suppuration of the bladder.

Amphotropin*. Popp tried this drug (hexamethylenetetramine camphorate) on himself for the treatment of cystitis. He took amphotropin as a bladder antiseptic as the operation on the prostate revealed the presence of an exceptional hypertrophy of the wall of the bladder. Under the influence of this drug the urine, which contained threads of pus, became clear in the course of a few days, the strangury abated so that the night rest was not disturbed; and less frequent irrigation of the bladder was necessary.

Hetralin (resorcin-hexamethylenetetramine)** was used by V. Drucker in the course of eighteen months in a large

* Compare Merck's Report 1912, p. 224.

Popp, *Ärztliche Mitteilungen* 1913, No. 24.

** Compare Merck's Reports 1903, 1904 and 1906.

Drucker, *Zentralblatt für die gesamte Therapie* 1913, No. 8, p. 393.

number of cases. In gonorrhoea of the urethra and bladder he observed a good result in that the tenesmus and the manifestations of irritation of the bladder often improved after one or two days' use of the drug. However, hetralin had no action on the gonococci. The action of hetralin is most marked in acute catarrh of the bladder secondary to gonorrhœal cystitis, chill, stricture of the urethra, hypertrophied prostate, paresis of the bladder of a central nature, tabes, myelitis, etc., in that the strangury, pains and dysuric symptoms disappear within a short time and the urine becomes clear. Hetralin is also useful as a symptomatic in phosphaturia, chronic inflammation of the bladder, cystitis in sufferers from disease of the prostate, and cystitis calculosa, although local intervention cannot be dispensed with in these affections.

Histopin.

The statements of Ledermann and Beck induced M. Joseph to try histopin in a large number of cases of staphylococcal infections of the skin. He found that the preparation is undoubtedly a prophylactic to fresh staphylococcal infections, and therefore in the treatment of furunculosis he lays great weight upon the immunising effect of the remedy on the neighbourhood of the furuncles. For this purpose about 1 c.c. of histopin gelatin is applied twice daily and this amount is spread over the area of the skin to be protected by means of a pledget of cotton wool. This treatment is continued for at least a fortnight, whereupon the remedy is applied once daily for a further period of eight days. Although this treatment often fails since it is usually adopted too late, it never causes any injury. The ointment is useless when necrosis has set in. On the other hand, in the superficial folliculitis of impetigo simplex histopin displays not only an immunising but also a curative effect, provided no streptococci are present. The action of histopin is more favourable in impetigo contagiosa. When the older method of treatment fails and when the use of 10 p.c. white precipitate ointment proves ineffectual, Joseph advises the use of histopin ointment, as he has obtained successful results even in severe forms. The use of

Ledermann, Merck's Report 1911, p. 264.

Beck, Merck's Report 1912, p. 224.

Joseph, Deutsche medizinische Wochenschrift 1913, No. 5, p. 203.

histopin gelatin is recommended in pemphigus vulgaris, since even in severe cases it frequently inhibits the local spreading of the bullæ, whereas histopin ointment is of use only as an adjuvant to the customary treatment. Histopin gelatin is also useful as a prophylactic in certain stages and forms of eczema, for instance in chronic eczemas of the hands where for unknown reasons suddenly acute exacerbation with all the symptoms of a reactive inflammation occurs, and superficial suppurating pustules appear in groups on circumscribed foci. Histopin ointment is employed to heal impetiginous eczema. Further, the author used histopin with successful results in eczema of the lips, acne vulgaris and varioliformis, perionychial eczemas, and also in blepharitis ciliaris. An equally favourable opinion of histopin is expressed by W. Bernheim and E. Saalfeld.

C. Hamburger has used histopin ointment with satisfactory results for the treatment of hordeola in chronic blepharitis, in eczematous keratoconjunctivitis and marginal phlyctenæ. In his experience it can be applied without apprehension to the palpebral margins and introduced into the conjunctival sac. It causes slight smarting, which can be prevented by previously instilling cocaine. R. Vollert also reports good results from the use of histopin ointment in the treatment of hordeolum and blepharitis ciliaris.

Hordenine Sulphate.

Charmoy reports on the use of hordenine sulphate* in veterinary practice. He administered it in fifteen cases to dogs suffering from simple diarrhœa or dysentery, and in thirteen cases he obtained a complete success. He injected a 5 p.c. solution of the drug subcutaneously into the chest or abdomen, in doses of 0.03 to 0.04 gramme for every kilogramme of body-weight. He states that the animal became

Bernheim, *Therapeutische Monatshefte* 1913, No. 6, p. 423.

Saalfeld, *Berliner klinische Wochenschrift* 1913, No. 24, p. 1113.

Hamburger, *Klinische Monatsblätter für Augenheilkunde* 1913, Vol. 51, p. 813.

Vollert, *Münchener medizinische Wochenschrift* 1913, No. 30, p. 1658.

Charmoy, *Recueil de médecine vétérinaire d'Alfort*, December 15, 1912, *Berliner tierärztliche Wochenschrift* 1913, p. 401.

* Compare Merck's Index 1910, p. 141 and Merck's Reports 1906, p. 128 and 1909, p. 231.

restless immediately after the injection, respiration became more frequent, tendency to vomit and vomiting occurred which lasted for some minutes. Hordenine is free from toxic action, and its effect is due to inhibition of peristalsis and of secretion. Charmoy's results are in agreement with those of Parent, who also employed hordenine in intestinal inflammation in a horse and in a dog.

Ichthargan.

In an interesting work P. G. Unna discusses the therapeutic properties of, and the indications for, ichthargan. From this exhaustive contribution only those statements will be briefly abstracted which it may be assumed are not generally known to dermatologists.

Ichthargan is an excellent remedy for psoriasis. If a part of the skin affected by this disease is treated with a 5 to 10 p.c. ichthargan ointment, only the healthy skin is darkened by the reduction of the silver salt, while the affected areas of the skin remain white. Only as healing progresses do these parts darken and the appearance of a homogenous silver discoloration denotes complete healing. However, this result is not obtained in every instance, even on using a 20 p.c. ointment. Therefore, if after two or three weeks a marked improvement but no cure has been achieved, the author proceeds to use chrysarobin, pyrogallol and tar, which display a quicker effect if employed after a course of ichthargan treatment. The reason why preference is given to ichthargan over the other three remedies at the beginning of treatment is due to the fact that it is harmless and less toxic. Unlike chrysarobin it does not cause acutely painful erythemata and inflammation of the eyes, therefore in cases where psoriasis is localised in the neighbourhood of the eye it can be used in the place of pyrogallol and tar, which are otherwise employed as substitutes for chrysarobin. Further, it has the advantage over these of not being a poison for the blood and does not penetrate deeper than into the upper layer of the cornea. It is also non-injurious to the kidneys, and for this reason may be used in patients suffering from albuminuria who are affected with psoriasis and cannot tolerate pyrogallol owing to its deleterious

Parent, communicated by Charmoy.

Unna, Medizinische Klinik 1913, No. 30, p. 1205 and No. 31, p. 1245.

effect on the kidneys. The absence of irritant action enables ichthargan to be used without interruption, and compared with chrysarobin it has the advantage of effecting a reliable disinfection of the entire skin, thereby excluding the possibility of a recurrence on the healthy skin, which is irritated by the application of chrysarobin. If necessary, ichthargan may be combined with other remedies employed for the treatment of psoriasis.

A further indication for ichthargan is afforded by dry seborrhoeic and callous eczemas, especially the latter, in which the customary remedies often not only fail but frequently cause an aggravation of the condition. Ichthargan may be included among the best remedies, such as pyraloxin, bismuth oxychloride and fluid extract of rhubarb, and according to Unna it is beyond doubt the most powerful. As far as possible the callous areas of the skin should be kept under the action of ichthargan until a cure is effected, for which purpose ichthargan guttaplast may be used. It allays itching and displays a curative effect.

Finally, ichthargan has assumed special importance in the treatment of chronic eczemas of the hands and fingers, such as the various occupation eczemas of masons, tradesmen, compositors, etc., which place great demands on the patience of both doctor and patient. The inconveniences experienced by those suffering from such eczemas are immediately removed by the application of ichthargan guttaplast. Recent, mild cases heal already within a few days, old-standing chronic cases require two to three weeks. The author points out that ichthargan displays a powerful action which ensures a good prognosis.

Ichthargan displays a good action also in hard warts on the hands and face, and in five cases Unna succeeded in effecting a complete cure in from eight to fourteen days by applying ichthargan guttaplast to the warts. The blackening of the skin can be removed by treating with Lugol's solution and solution of sodium thiosulphate.

For the treatment of hæmaturia in horses R. Schmidt advocates intravenous injections of ichthargan (1 gramme [15 grains] in 30 grammes [1 oz] of boiled water), which he found were quite harmless to the organism. In severe cases in which

the animals were passing dark red urine, with a temperature of 41° C., diarrhoea, weakness and complete loss of appetite, already five or six hours after the injection the appetite returned, the fever abated and the urine was free from blood pigments. The injection may be repeated without apprehension after six and twelve hours; in the cases recorded by the author one injection always proved sufficient. Ichthargan injections are also useful in anthrax. In giving an intravenous injection care must be taken to avoid loss of blood and the injection must be made into the vein, as ichthargan would display a caustic action on the wall of the vein and connective tissue.

Ichthyol.

According to S. Gross, acne rosacea is frequently associated with affections of the nasal mucous membrane, and after these have received suitable treatment the redness of the nose disappears. He therefore draws attention to the value of ichthyol, which is also useful in the transient redness of the nose occurring in young girls (erythema fugax nasi) as an angio-erethistic manifestation. He prescribes:

Ferr. lact. 10 grammes ($\frac{1}{3}$ oz)

Ichthyol 10 grammes ($\frac{1}{3}$ oz)

Ext. et rad. glycyrrh. q. s. ut ft. pil. 100.

Saynisch employs ichthyol in combination with arthigon (gonococcus vaccine) for the treatment of gonorrhœal epididymitis. He adopts the following procedure: The patient is made to rest in bed and the affected half of the scrotum, and the area of skin in the region of the spermatic cord as far as the umbilicus, are painted with pure ichthyol, and then covered with a piece of ordinary cotton wool not freed from fatty matter; a well fitting suspensory is applied over the whole. The ichthyol dressing is renewed after three or four days, after removing the old dressing with warm water. With this treatment the inflammatory manifestations soon subside, as well as the pain and swelling; the nodules, which are absorbed with difficulty, become smaller or disappear entirely, so that the patient is able to resume his occupation after a short time. In addition to the use of ichthyol ice compresses are applied, although it might be objected that the application

Gross, Medizinische Klinik 1913, No. 25, p. 981.

Saynisch, Deutsche medizinische Wochenschrift 1913, No. 40, p. 1942.

of ice would favour the formation of nodules difficult of absorption. This possible deleterious action of ice is completely removed by the use of ichthyol, arthigon, and if necessary, of fibrolysin. On the following day an intravenous injection of arthigon is made, provided the temperature is not higher than 38° C., in which case arthigon is given intramuscularly until the temperature admits of intravenous injection. The initial dose is 0.1 gramme, increasing within seven days to 0.4 gramme; in all four syringefuls are given and this amount is usually sufficient. With this treatment the author obtained very good results.

In furunculosis ichthyol may be advantageously combined with iodine, as is apparent from F. Berger's report. According to his directions, soft furuncles, as well as the surrounding healthy skin, are painted with tincture of iodine, whereupon a compress covered with a thick layer of 10 p. c. ichthyol-vaseline is applied. On the following day the pus which has escaped is removed, and the skin is cleansed with benzin, to prepare it for a fresh coating of tincture of iodine, followed by the renewed application of an ichthyol dressing. As soon as the pus from the furuncle is absorbed or has escaped outside, disinfection with iodine may be suspended and treatment is continued with ichthyol-vaseline or with pure ichthyol. Towards the end of treatment, in order to hasten the formation of skin over larger defects (which as a rule never occur with the use of ichthyol), an ointment consisting of 5 grammes (75 grains) of balsam of Peru, 1 gramme (15 grains) of silver nitrate and 94 grammes (3¼ oz) of lanoline may be applied. However, the real sphere of usefulness of this treatment is afforded by hard nodular furuncles, furuncular foci which have not become soft, and incipient staphylogenic folliculitis and perifolliculitis. In these cases energetic treatment with tincture of iodine and pure ichthyol is required, which yields excellent results and prevents re-infections. For details the original paper should be consulted.

Since calcium salts and ichthyol play a not unimportant part in the treatment of pulmonary tuberculosis, C. Schütze's experience with calcium ichthyolate is doubly interesting. The author employed ichthyol with the object of avoiding un-

Berger, Medizinische Klinik 1913, No. 46, p. 1889.

Schütze, Medizinische Klinik 1913, No. 37, p. 1502.

pleasant secondary effects referable to the intravenous injection and not with the definite view of combining both preparations. He used a 5 p.c. solution of calcium ichthyolate, of which injections of 5 c.c., repeated several times a week, caused neither a rise of temperature nor abscess formation at the site of injection. The author prepared his calcium ichthyolate from ichthyolsulphonic acid and calcium hydroxide, the resulting product is soluble in water and contains 7.8 p.c. of calcium, so that 5 c.c. of the above mentioned solution contain 0.0195 gramme of calcium. According to Schütze, the use of this solution causes the temperature to return to normal, stimulates phagocytosis and improves the general condition of the patients.

Indicators for Volumetric Analysis.

o-Dioxydibenzalacetone (lygosin) forms pale yellow crystals* which are soluble in alcohol. It has the chemical formula



According to A. Ferencz, a 1 p.c. alcoholic solution is used as an indicator, which produces a pale yellow colour with acids (in larger amounts it produces an opalescent precipitate). With alkalis it produces an orange-red colour. For titration 3 to 4 drops of the indicator should be used for 100 c.c. of liquid. According to the author's report this indicator is as sensitive as phenolphthalein. It is not to be recommended for titrating ammonia since the change of colour takes place too slowly.

Dibromo-*o*-*o*-dioxydibenzalacetone shows the same behaviour as an indicator as dioxydibenzalacetone, but is less suitable for use since it is less soluble in water and therefore the addition of the 1 p.c. alcoholic solution to an aqueous acid liquid causes a precipitate even with small amounts.

For titrating the alkalinity of serum lacmoid paper is generally used, which is well-known to be one of the most delicate indicators. A very useful indicator for the same purpose

* Compare Fabinji's lygosin (diortho-coumar-ketone) in Merck's Report 1900, p. 133.

Ferencz, Pharmazeutische Post 1913, No. 49, p. 521.

is also neutral red paper, with which J. Snapper obtained very good results. As a stock solution he used a concentrated alcoholic solution which he diluted before use with ten times the amount of alcohol (50 p. c.). Filter paper is well moistened with this solution and dried for half an hour in an incubator. Not more paper should be prepared than is required during the day. It is used for carrying out the drop test, as the change of colour in solutions is not sufficiently clear. As the author says nothing about the change of colour, it may be mentioned that an alcoholic solution of neutral red has a fuchsine-red colour, and with it a red paper is obtained, which assumes a brownish colour with alkalis, and with acids a blue colour.

Bilberry Juice, which is neutralised as much as possible, is said by G. N. Watson to be a good indicator for use with $\frac{1}{50}$ normal solutions. The indicator is coloured red by acids and olive-green by alkalis.

Red Cabbage Juice. The red cabbage indicator used by Walbum as an indicator for fluids containing albumin yields a similar change of colour. It is obtained by extracting 500 grammes of finely cut red cabbage with 500 grammes of alcohol (96 p. c.) for forty-eight hours, and filtering the red liquid thus obtained. 5 to 10 drops of this indicator are added to 10 c. c. of the fluid to be titrated. The sensitiveness of the indicator is satisfactory even in the presence of large amounts of genuine albumin.

Diphenylcarbazide* was employed by O. L. Barnebey and S. R. Wilson as an indicator in the titration of ferrous salts with dichromate. As an indicator a solution of 1 gramme of diphenylcarbazide in 1000 c. c. of glacial acetic acid is used. To the solution of ferrous chloride, or of ferric chloride reduced by stannous chloride, to be titrated definite amounts of manganous sulphate, mercuric chloride and hydrochloric acid are added, and titration is carried out with solution of potassium dichromate after the addition of

Snapper, *Biochemische Zeitschrift* 1913, Vol. 51, p. 88.

Watson, *American Journal of Pharmacy* 1913, Vol. 85, p. 246.

Walbum, *Biochemische Zeitschrift* 1913, Vol. 48, p. 291.

* Merck's Reports 1900, p. 88; 1904, p. 59; 1906, p. 95; 1909, p. 187.

Barnebey-Wilson, *Journal of the American Chemical Society* 1913, Vol. 35, p. 156.

3 c. c. of solution of diphenylcarbazide. The mixture at first assumes a red to purple colour and the end point is apparent by a faint green coloration which is easily recognized. Since diphenylcarbazide itself acts as a reducer, the amount of dichromate solution required for its oxidation must be subtracted.

Inulin.

Strauss advanced the view that inulin (elecampane starch) deserves wider recognition in the treatment of diabetes mellitus, and during the past year R. Roubitschek, O. Gaupp and A. Goudberg have reported upon its use.

Roubitschek and Gaupp prescribed it for five diabetics, in three cases of moderate severity and in two mild cases. In two cases a striking success was obtained, for the excretion of sugar was reduced from 18 grammes to 6.6 grammes, and from 45 grammes to 38 grammes; while the amount of NH_3 after the use of inulin dropped from 1.56 to 0.26, and in the other case from 1.97 to 0.60. On the other hand, the amounts of acetone remained almost unchanged. In the other three cases inulin proved ineffective. Of these two showed no influence on the excretion of sugar; while one case, which had become free from sugar before the use of inulin, became even worse, for two days after beginning inulin administration with standard diet the excretion of 60 grammes of sugar was observed. In these three cases the amounts of NH_3 and of acetone also remained uninfluenced, and in two of the cases the acidosis was reduced only after a course of oatmeal.

Basing on his experiments, Goudberg concludes that inulin is a carbohydrate which is oxidised and is well utilized in the human organism, and therefore deserves wider recognition in the treatment of diabetes.

Iodine.

B. Reich-Brutzkus states that the application of iodine before operations is the best method of disinfection at present available; it is convenient, reliable and easily carried out.

Strauss, Merck's Report 1912, p. 240.

Roubitschek-Gaupp, Medizinische Klinik 1913, No. 26, p. 1040.

Goudberg, Zeitschrift für experimentelle Pathologie und Therapie 1913, Vol. 13, p. 310.

Reich-Brutzkus, Wiener klinische Rundschau 1913, No. 16, p. 244.

According to the authoress' report a modification of Grossich's* procedure was used in 100 cases. The field of operation was painted with a solution of 3 grammes of iodine in 10 grammes of absolute alcohol and 90 grammes of chloroform, which was allowed to act for at least five minutes, after which the skin was rubbed with alcohol (96 p. c.). However, the healing of the wound showed no clinical difference if the cleansing with alcohol were performed before the expiration of five minutes, but if this time is allowed to elapse eczemas may be prevented. Disinfection with iodine was not adopted in children under five years of age.

For disinfecting the skin Crucilla prefers a 6 p. c. alcoholic solution of iodine, which should be prepared freshly each time before use to prevent the formation of hydriodic acid on keeping. He paints the skin of the field of operation with this solution twelve minutes before the operation, and in persons with a delicate skin two or three minutes before the operation. To avoid irritation through the formation of iodide of mercury no compresses impregnated with solution of mercuric chloride should be applied before painting with the iodine solution. In places where two surfaces of the body which have been painted with iodine are liable to touch each other, isolation should be effected by means of gauze. Heinemann succeeded in preventing any irritation due to iodine by rubbing the parts of the skin previously painted with iodine after the operation with a mixture of 5 grammes of solution of ammonia, 45 grammes of ether, and 50 grammes of alcohol.

The popularity of tincture of iodine, particularly of a 5 p. c. solution, for disinfecting the skin before operations is abundantly proved by the replies received from leading surgeons in response to an enquiry instituted by the "Medizinische Klinik", and which were published in No. 12, 1913, page 453. The following have expressed themselves in favour of its employment: W. Körte, Kocher, Küttner, Kümmell, V. Lieblein, W. Müller, E. Enderlen, C. Ewald and J. Schnitzler.

* Compare also Tokarski, Wiener medizinische Wochenschrift 1913, No. 46.

Crucilla, Gazzetta degli ospedali e delle cliniche 1913, No. 25.

Heinemann, Zentralblatt für Chirurgie 1913, No. 46, p. 1773.

On the other hand, E. Schuster deprecates the use of tincture of iodine for disinfecting the oral mucous membrane, since in the mouth it is impossible to comply with Grossich's principal conditions demanded by him for his method, i. e., the iodized skin cannot be protected by an aseptic dressing, moisture cannot be excluded, and iodized surfaces cannot be prevented from coming into contact with one another. Moreover, painting with iodine causes loss of substance of the epithelium, which exerts an unfavourable influence on the healing process. E. L. Fieber also rejects the method of painting the mucous membranes with iodine in operations on the gastro-intestinal tract, since he observed in one case necrosis in the region of the sutures after the use of iodine. On the other hand, J. Hohlbaum states that in a large number of cases painting of the mucous membranes with iodine never gave rise to even the slightest suspicion of sutural insufficiency or of necrosis of the intestinal wall. The results of three cases of tuberculous peritonitis treated with tincture of iodine induce A. Falkner to express a favourable opinion of the use of tincture of iodine. One was a case of dry and the other of moist peritonitis, and in both painting with iodine shortened the healing process without causing any injury whatever. In the moist case tincture of iodine, and in the dry case iodine-vasogen, was used and the treatment was assisted by enemata of iodipin. In spite of Rovsing's aversion to the use of tincture of iodine, the author accepts Bier's view that iodine exerts a healing action on the tuberculous tissues. However, he leaves it an open question whether in the adhesive forms preference should not be given to the use of oily substances, such as iodipin, in the place of iodine. Further experience is required to elucidate this point.

S. Stocker is also in favour of the use of tincture of iodine in dry tuberculous peritonitis. From experiments on animals he gained the impression that iodine exerts a directly healing influence on the tuberculous process and that the fear of the formation of adhesions from its use is unfounded.

Schuster, Deutsche zahnärztliche Wochenschrift 1913, No. 18, p. 322.

Fieber, Zentralblatt für Chirurgie 1912, No. 34, p. 1161.

Hohlbaum, Zentralblatt für Chirurgie 1913, No. 10, p. 344.

Falkner, Münchener medizinische Wochenschrift 1913, No. 18, p. 978.

Stocker, Schweizer Rundschau für Medizin 1913, Vol. 13, p. 745.

He was able to demonstrate the value of iodine treatment in two cases in his practice.

Jochmann and F. W. Strauch report on the disinfection of the cervical organs with tincture of iodine. Jochmann, who tried it in a large number of cases, was unable to achieve satisfactory results, whereas Strauch believes that systematic painting with iodine in diphtheria should prove very effective. He treated fifty cases of diphtheria, some of which were severe cases, with iodine after injecting anti-toxin. If about eight days after the diphtheritic membranes had been thrown off bacilli were still demonstrable in the swab from the tonsils, he undertook a systematic painting of the pharyngeal tonsils with 10 p. c. tincture of iodine to effect their complete removal. Of the fifty cases twenty were freed from bacilli after three days' painting with iodine, sixteen after from one to two days, and four after four days' treatment. Four particularly severe cases of nasopharyngeal diphtheria proved refractory to this treatment. This treatment did not cause any pain or other unwelcome secondary effects (erosions). In the presence of complications, such as high fever, nephritis, etc., the painting was not resorted to. As this treatment may in many instances prevent the patient from becoming a carrier of infection it is worthy of wider recognition.

According to D. Rothschild, W. Weil and Holz, iodine treatment is useful in tuberculosis since it causes lymphocytosis. Holz in particular undertook a clinical study of this method of treatment. In tuberculosis of the bones and soft parts the affected parts were opened by a wide incision and curetted, and then rubbed with tincture of iodine, whereupon an iodoform plug was inserted and the wound closed. In addition, iodine was supplied to the organism by painting extensive areas with tincture of iodine. In the great majority of his cases the author obtained excellent results by this method. Rothschild employed iodine internally, and also sub-

Jochmann, *Ergebnisse der inneren Medizin und Kinderheilkunde* 1913, Vol. 11, p. 793.

Strauch, *Therapie der Gegenwart* 1913, No. 21, p. 390.

Rothschild, *Deutsche medizinische Wochenschrift* 1913, No. 25, p. 1196.

Weil, *Zeitschrift für Chemotherapie* 1913, p. 412.

Holz, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, Vol. 25, No. 1.

cutaneously and intravenously in the shape of iodoform. He gave iodoglidine internally and iodipin (25 p. c.) subcutaneously. One intragluteal injection of 5 to 10 c. c. ($1\frac{1}{2}$ —3 dr.) sufficed for three weeks, since with this amount of iodipin deposited in the body a fairly constant excretion of iodine in the urine was maintained for a period of three weeks. If a prompt action is desired, an ethereal solution of 0.015 to 0.06 gramme ($\frac{1}{4}$ —1 grain) of iodoform is injected intravenously three times weekly (according to Dewar). The dose is decreased in the presence of toxic symptoms such as a rise of temperature and increased expectoration. With this treatment the author succeeded in four cases in causing the disappearance of the bacilli in the sputum within three months.

J. Pakowski gives detailed directions for making the injections of iodine in synovial cysts of the wrist-joint. After painting the site of injection with tincture of iodine he injects two to three drops of tincture of iodine into the cyst and then applies a light compression bandage. On removing the bandage after five days the cyst usually appears smaller. This treatment is repeated once or twice, but as a rule the cyst has disappeared after the second injection. In view of the simplicity and painlessness of iodine injections and their excellent action, the author states that they are worthy of wider recognition.

Thederling states that tincture of iodine is a useful preparation in herpes tonsurans. He gives the following procedure: The focus is painted for four days morning and evening with tincture of iodine, without previously cleansing it with soap. On the following two days, to dissolve the iodine crust which has formed, an ointment is rubbed in consisting of 1 gramme (15 grains) of salicylic acid, a little olive oil and sufficient lanoline to make 30 grammes (1 oz), also without previous cleansing with soap. On the seventh day the now softened iodine crust is removed by washing once with soap and water. This procedure is repeated until a cure is effected.

The successful results obtained by painting with iodine in small-pox, reported by Rockhill in the preceding year,

Pakowski, Progrès médical 1913, No. 10.

Thederling, Münchener medizinische Wochenschrift 1913, No. 48, p. 2679.

Rockhill, Merck's Report 1912, p. 242.

have been confirmed by E. Cabanès, A. G. Newell and T. F. Pedley, who obtained uniformly very satisfactory results from the application of tincture of iodine. The method of iodine fumigations for disinfecting the bladder proposed by Farnarier has also found a supporter in S. Pascual, who always obtained the desired result in cystitis. He allowed the iodine vapours to act for two to three minutes in the bladder; this treatment was repeated every second day and in the beginning caused pain.

In gastric and intestinal hæmorrhages Nottebaum prescribed the internal use of tincture of iodine:

Rp. Tinct. iod.	min. xxv
Sod. iodid.	0.1 gramme ($1\frac{1}{2}$ grains)
Aq. menth. pip.	
Syrup.	aa 20 grammes ($\frac{2}{3}$ oz)
Aq. dest.	ad 200 „ (7 oz).

At first he gave one tablespoonful of this mixture every half hour, later hourly or every two hours. This treatment is said to yield very prompt results also in intestinal bleeding in typhoid. This mixture is also useful in the prominent symptoms of gastric ulcer, especially in painfulness to pressure in the gastric region. It may be used combined with bismuth subnitrate as a mixture to be shaken before taken. In chronic cases he prescribes:

Rp. Tinct. iod.	2 grammes (40 min.)
Tinct. amar.	13 „ ($\frac{1}{2}$ oz)
M. Sig.:	10 to 15 drops to be taken in chamomile tea, before meals.

In eye work Jacqu eau used ordinary tincture of iodine to which he added 3.75 p. c. of potassium iodide so as to be able to dilute it with water, if necessary, without causing the iodine to precipitate. It is useful especially in infectious ulcers of the cornea, affections of the eyelids (blepharitis),

Cabanès, Newell, Pedley, *Semaine médicale* 1913, No. 7, p. 79 and *Revue internationale de médecine et de chirurgie* 1913, No. 2, p. 30.

Farnarier, *Merck's Report* 1912, p. 242.

Pascual, *Zentralblatt für die gesamte Chirurgie* 1913, Vol. 3, p. 663.

Nottebaum, *Deutsche medizinische Wochenschrift* 1913, No. 49, p. 2409.

Jacqu eau, *Lyon médicale* 1913, No. 17. — *Klinisch-therapeutische Wochenschrift* 1913, No. 42, p. 1282.

and as an antiseptic after operative procedures. In ulcers of the cornea a little solution of cocaine (1:20—30) should be instilled before applying iodine. The antiseptic action of tincture of iodine is particularly useful in operations for cataract; before the operation the palpebral margins are wiped with it and after the operation the site of the incision is treated in the same way. A. Dutoit recommends the internal use of iodine in the prophylaxis of glaucoma. The author gave for several years small doses of potassium iodide.

O. Schewket describes a colour reaction of gallic and tannic acids and its practical employment. If 3 c. c. of a 1 p. c. solution of iodine and potassium iodide are mixed with 2 c. c. of a 1 p. c. solution of gallic or tannic acid and 300 to 500 c. c. of tap-water are added, a mixture is obtained with a beautiful reddish-violet colour. This reaction is produced by those constituents in the water having an alkaline reaction. As a test for alkalinity the author proposes the following reagent:

- a) 1 gramme of iodine and 2.5 grammes of potassium iodide are dissolved in 100 c. c. of water;
- b) 1 gramme of tannic acid is dissolved in 100 c. c. of water.

Three drops of each of these two solutions are mixed with 10 c. c. of distilled water and 10 c. c. of the liquid to be tested are added. A dirty brown coloration denotes the presence of caustic alkalies or of a concentrated solution of an alkaline carbonate; a reddish-violet coloration denotes very dilute alkalies or salts with an alkaline reaction, such as phosphates and borates. If the solution to be tested is rendered faintly acid towards litmus with 0.1 c. c. of normal hydrochloric acid, so that the acid reaction persists on heating to boiling, and is strongly diluted with water and, after cooling, submitted to the above test, the production of the reddish-violet coloration shows that salts of organic acids are present. By modifying it in a suitable manner the iodine reaction may be used to distinguish mineral and organic acids, and also to demonstrate the presence of gallic and tannic acids in plants and pharmaceutical preparations.

Dutoit, *Zeitschrift für Augenheilkunde* 1912, p. 131.

Wochenschrift für Therapie und Hygiene des Auges 1913, Vol. 16, No. 35, p. 286.

Schewket, *Biochemische Zeitschrift* 1913, Vol. 52, p. 271.

Iodipin.

E. Hoefler gives some valuable hints regarding the use of iodipin in practice, which should prove useful especially for its subcutaneous injection. In the first place a suitable syringe is required with a capacity of 10 c. c. (3 dr.) and provided with a needle 10 cm. (4 in.) in length, of medium calibre, so that undue force is not necessary in making the injection. With one syringeful it is possible to incorporate 0.6 to 2 grammes (9—30 grains) of organically bound iodine, according to whether 10 or 25 p. c. iodipin is employed; this amount is equivalent to that given in the customary mixtures. For the site of injection, speaking in strictly anatomical terms, the gluteal region should not be selected, but the sacral and perineal region along a line which marks the depression of both gluteal prominences into the anal groove. By selecting this site of injection it is possible to obviate the often unwelcome secondary effects which are sometimes produced by a deep puncture into the gluteus maximus. The site of injection is first disinfected by rubbing with ether, or painting with tincture of iodine. Special care should be taken to keep the needle clean, while this is of minor consequence with the syringe since iodipin is per se sterile. If one wishes to avoid boiling the needle before each injection, a set of five to ten needles can be kept ready for use in alcohol, from which a needle is taken immediately before making the injection, and afterwards immediately replaced in the alcohol. If the needles are placed upright in the alcohol the iodipin they still contain flows out and in time discolours or causes cloudiness of the alcohol, which is then renewed. The author states that it is superfluous to remove the syringe from the needle after making the injection as at the above mentioned site of injection larger vessels cannot be reached by a needle 10 cm. in length, since they lie at a greater depth. He states that it is not necessary first to warm the iodipin to body temperature as it is quite sufficient if it is injected at the temperature of the room, and if the site of injection is properly selected the iodipin is borne without discomfort even if not warmed above the ordinary temperature. After injecting, the skin over the puncture is briefly massaged with a pledget of cotton wool

to hasten absorption of the iodipin. If a little blood escapes the site is compressed with cotton wool, which is frequently renewed, until no more blood appears. This procedure has the advantage that the occurrence of secondary hæmorrhage need not be feared. Finally the puncture is covered with a pledget of cotton wool the size of a pea, which is held in place by a strip of adhesive plaster. It may be mentioned that Hoefler prefers making the injections of iodipin with the patient lying flat on the abdomen, as in this position any bleeding which may occur is more easily controlled, while it is also more convenient for the doctor. In regard to dosage, an injection of 10 c. c. (3 dr.) of iodipin 25 p. c. every third day should prove sufficient; it is not advisable to inject more than 200 c. c. (7 oz) for one course of treatment. The sole contraindication to iodipin would be febrile conditions, with the exception of diabetes, in which the author never observed any disturbances.

The technique of iodipin injections and their indications are also discussed by H. Bosse. In his experience iodipin proved an effective remedy in various affections which are otherwise difficult to influence, and he found it especially useful in diseases of the heart and vessels, and in septic and pyæmic processes. The use of iodipin never proved harmful and he scarcely ever observed it to fail. Special interest attaches to a case of septic gonorrhœa described by the author which had undergone various forms of ambulatory and clinical treatment and only showed an improvement after iodipin was employed. After one injection of 10 c. c. (3 dr.) of iodipin the temperature became normal and the patient quickly recovered. He remained afebrile and the slightly catarrhal condition of the lungs which was present disappeared also within a short time. According to Bosse, the injection of iodipin displayed so prompt an action that there was no room for doubt as to the effect of the drug on the septic process.

E. von Bassewitz also discusses the technique of iodipin injections and their indications, and he gives case-histories from his practice which confirm the value of iodipin, especially in syphilis.

A case of actinomycosis which was cured by iodipin treatment is described by F. Bittner and J. Toman. The case was that of a robust woman, aged 36, who suffered from pains and swelling of the external auditory canal and mastoid process, as well as from attacks of suffocation due to swelling of the pharynx. The diagnosis was made a fortnight later from the pus after the operation; in the meantime the infiltration, which was as hard as a board, had descended towards the lower end of the musculus sternocleidomastoideus. The authors commenced with daily subcutaneous injections of sodium cacodylate, beginning with a dose of 0.1 gramme ($1\frac{1}{2}$ grains) and slowly increased the amount to 1 gramme (15 grains), then decreasing to 0.1 gramme ($1\frac{1}{2}$ grains). At the same time, after the first incision, iodipin 25 p. c. was injected into the infiltration. The injection was painless, the second injection repeated two weeks later caused pain after two hours and the infiltration began to swell. These symptoms passed off after the application of compresses dipped in solution of aluminium acetate. A further injection proved painless. The broken down tissues always escaped through the small incision. The wound healed and the infiltration disappeared leaving only a slight scar.

Iodipin is also useful in the treatment of lupus. In one case, instead of excochleation of the constantly recurring lupus nodules, the authors injected iodipin 25 p. c. under the nodules by means of a Pravaz syringe, whereupon the nodules disappeared and it was no longer necessary to scrape them out. In addition to iodipin sodium cacodylate was injected in increasing and then decreasing doses.

Iodipin has also proved useful in prostatitis. In the place of the customary irrigations according to Arzberger and the use of ichthyol and potassium iodide suppositories, which often cause tenesmus, L. Fischel prescribed iodipin in the form of enemata. The latter are free from the drawbacks coupled with the use of the above mentioned suppositories, they display a prompt and beneficial action on acute and long-standing cases of prostatitis in that they promote the absorption of the infiltration or cause the hardened tissue to become softer. The author adopts the following procedure: A mixture of

Bittner-Toman, Prager medizinische Wochenschrift 1913, No. 27.

Fischel, Münchener medizinische Wochenschrift 1913, No. 12, p. 651.

100 grammes ($3\frac{1}{2}$ oz) of iodipin 25 p. c. and 200 grammes (7 oz) of olive oil is prepared, of which 10 c. c. (3 dr.) are slowly injected into the rectum by means of a syringe with a capacity of 10 c. c. A small piece of cotton wool is then applied to the opening of the anus. The patient retains the enema without inconvenience, whereby about 0.75 gramme (11 grains) of iodine are incorporated. The injection is repeated daily or every second day. With this treatment an improvement in the symptoms of the prostate is frequently observed already after one week. Occasionally increased secretion again occurs, the second portion of urine commences to become clearer, and after two to three weeks the prostatitis has completely disappeared, or if a few symptoms still remain these are easily removed by massage or by a few irrigations. Although some cases may not yield to this treatment, however, the very great percentage of successful results obtained in the cases so treated fully justifies a trial with this method, all the more so since it is simple, painless and easy of application.

As I have already stated* elsewhere, Berliner proposed the use of injections of menthol and eucalyptol in the treatment of tuberculosis. In the place of the dericin oil used as a vehicle and solvent iodipin may be employed with advantage, as here its antiphlogistic effect and property of dissolving mucus are displayed in addition to the action of menthol and eucalyptol. The following prescription is used:

Rp. Menthol.	10 grammes	($\frac{1}{3}$ oz)
Eucalyptol.	20	„ ($\frac{2}{3}$ oz)
Iodipin 25 p.c.	50	„ ($1\frac{3}{4}$ oz)

M. Sig.: For injection.

1 c. c. (17 min.) of this mixture is injected into the buttocks daily for ten days. The following ten injections are made every second day, and the last ten injections at intervals of two days. The following case may be adduced; a patient came for treatment with slight dullness at the back of the upper right region of the thorax and with a somewhat pronounced inspiratory murmur. The left upper part exhibited somewhat diminished respiration with slight râles. The patient formerly had occasionally hæmoptysis. He was given

* Compare the article on Eucalyptol in this Report.

Berliner, Berliner klinische Wochenschrift 1913, No. 37, p. 1705.

altogether 21 injections. After the sixteenth injection the temperature had become normal, the right side showed no anomaly and in the left side only a slight ringing sound was heard. After a stay of six weeks in a convalescent home the patient was completely restored.

In the presence of irritation of the kidneys the author counsels caution. Smaller doses should be given and the treatment should be stopped if no diminution in the albuminuria is apparent. The injections of iodine and menthol are also useful in the treatment of tuberculosis of the bones and joints. In children it is advisable to begin with small doses, about one division, and then gradually increase the dose. By this means no harm can ever result.

O. Baer also records excellent results with the use of iodipin in the treatment of tuberculosis. In ten cases of open pulmonary tuberculosis of moderate severity he was able to observe a marked abatement in the symptoms after injecting iodipin. The patients' appearance improved, the hæmoglobin content of the blood increased, appetite and sleep improved, the temperature became normal and the feeling of lassitude disappeared. In addition, the râles, the cough and the expectoration diminished, respiration became quieter, and in seven patients no tubercle bacilli were demonstrable in the sputum at the end of the treatment. In two cases the albuminuria which was present also disappeared. The age of the patients treated ranged from 18 to 24 years. Three injections of 3 c.c. (50 min.) of iodipin 25 p.c. were given weekly until forty injections in all had been made. This treatment was always well borne and in no case did symptoms of iodism or headaches occur. Baer also confirms the beneficial influence of the menthol-eucalyptol-iodipin mixture proposed by Berliner, but he ascribes its action to the iodine.

The great value of iodipin was apparent also in other tuberculous affections. Baer injected iodipin in one case of tuberculous glands, in one case of hæmoptysis associated with thrombophlebitis, and in one case of pains in the shoulder due to infiltration of the lung with pleuritic adhesions, and always obtained a satisfactory result. Finally the author draws attention to the efficacy of iodipin in chicken-pox, tabes, chronic sciatica, and in anæmia associated with symptoms of

Graves's disease, cases of which he has treated successfully by injections of iodipin.

A. Falkner reports on the treatment of tuberculous peritonitis by preparations of iodine. In one case in which laparotomy showed the presence of indurated peritonitis and where a radical operation was not practicable owing to the poor state of health of the patient, the author poured 30 grammes (1 oz) of iodine-vasogen upon the tumour and closed the wound. In addition he gave enemata of iodipin. The patient recovered and a later examination revealed nothing abnormal in the abdomen.

According to L. Rehn, if iodipin is introduced into the pericardium it is capable of preventing, or restricting, the formation of adhesions in the pericardium. Therefore iodipin may prove useful in the surgery of the heart. It has not yet been employed in man. If it is capable of realizing the hopes raised by the results of experiments on animals, the author believes that its use will constitute a further advance.

Iodipin for Veterinary Use.

The use of iodipin in veterinary practice is discussed by W. Keith and R. Grimm.

Keith tried the remedy in six cases of morbus maculosus secondary to strangles and inflammation of the throat. In those cases which were favourably influenced repeated injections of 25 grammes ($\frac{5}{8}$ oz) of iodipin 25 p.c. effected a speedy improvement. The author lays stress upon the fact that larger abscesses never form at the site of injection, in contradistinction to the statements of other authors who have reported the formation of abscesses as a complication of iodipin treatment. He found that a flat swelling occurs after injecting a large dose of iodipin, and frequently small abscesses form which, as a rule, heal rapidly after being incised. On the other hand, he never observed necrosis of the skin or cellular tissue. Care should be taken to ensure the iodipin having the proper temperature when injected, and the injection should be made

Falkner, Münchener medizinische Wochenschrift 1913, No. 18, p. 979.

Rehn, Berliner klinische Wochenschrift 1913, No. 6, p. 245.

Keith, Österreichische Wochenschrift für Tierheilkunde 1913, No. 33.

Grimm, Tierärztliches Zentralblatt 1913, No. 9 — Compare Merck's Report 1908, p. 233.

under strict aseptic precautions. With regard to the value of iodipin in morbus maculosus the author comes to the conclusion that although it is not a specific it is, however, a valuable remedy in the treatment of this affection.

Grimm states that iodipin acts as a specific in tetanus in horses. He recently reported another case of a horse in which tetanus set in owing to the non-aseptic treatment of an operation wound. A subcutaneous injection of 50 grammes ($1\frac{2}{3}$ oz) of iodipin 10 p.c. was made, and this was repeated five days later. In addition, the wound which had been the point of entrance of tetanus was washed with a solution of creolin. Subsequently another injection of 15 c.c. ($\frac{1}{2}$ oz) was given and after a few weeks two injections of 30 c.c. (1 oz) of iodipin each, whereupon the animal recovered completely.

Iodocitin.

Jacobsohn used iodocitin* with satisfactory results in twelve cases, including cases of articular rheumatism, pulmonary tuberculosis, parametritis, glandular swellings, anæmia, arterio-sclerosis, neurasthenia, diabetes and syphilis. Of these, acute articular rheumatism is a new indication for iodocitin. In two cases the author obtained an improvement with iodocitin after all the other usual remedies had failed; the fever abated, the swellings decreased, the pains disappeared and the appetite improved.

H. Mayer prescribed iodocitin in syphilis after mercurial and salvarsan treatment, on the basis of the fact that in addition to the iodine the lecithin contained in the preparation is particularly useful. It replaces the loss of lecithin which takes place in pathological conditions, especially in syphilitic and metasymphilitic processes of the nervous system. Therefore at the conclusion of the mercurial and salvarsan treatment he prescribes one tablet of iodocitin three times daily.

Cramer undertook experiments with iron-iodocitin. He states that in this preparation, which is issued in tablet form, the iron and iodine are present in organic combination to which the lecithin is attached. Each tablet is equivalent to 0.0075

Jacobsohn, Allgemeine medizinische Zentral-Zeitung 1913, No. 28, p. 337.

* Compare Merck's Report 1911, p. 282.

Mayer, Dermatologische Wochenschrift 1913, No. 35, p. 1033.

Cramer, Deutsche medizinische Wochenschrift 1913, No. 22, p. 1045.

gramme of iodine and 0.0015 gramme of iron as well as 0.041 gramme of lecithin. Tablets are also supplied which in addition to iodine and iron also contain 0.0002 gramme of arsenic. The author prescribed these tablets for children of two and a half to six years of age, in anæmia, rickets and scrofula. The preparation was readily taken and was well borne; only one girl, aged five, exhibited loss of appetite, coryza and epistaxis while taking the tablets, so that the use of the remedy had to be stopped. The majority of the children showed an increase of appetite, a gain in weight and an improvement of the general condition as well as of the local processes. Children up to four years of age were given two tablets and older children three tablets daily.

J. Trebing also expresses a favourable opinion of the value of iron-iodocitin. In his experience it effects a marked regeneration of the blood picture in mild as well as severe cases of chlorosis, and also in various secondary anæmias. Owing to its content of iodine it displays a powerful absorbent action, while its lecithin content acts as a tonic, also on the nervous system.

Iodostarin.

G. Stümpke and E. Bäumer report their experience of iodostarin* in the treatment of syphilitic affections. According to Stümpke those cases of secondary syphilis react well to the preparation which, after the appearance of the general manifestations, are accompanied by severe headaches and pains in the joints and which are manifestly due to meningeal or periosteal irritation. Further, the preparation proved a valuable adjuvant to mercurial and salvarsan treatment in tertiary manifestations, and in some cases it still effects involution of specific manifestations when other antiluetic remedies fail to display a marked action. In tabes the author frequently observed a remarkably rapid cessation of the lightning pains, in addition to a favourable influence on the general condition. Iodism was a rare occurrence with iodostarin, and when it occurred it assumed a mild form. In the presence of slight iodine acne,

Trebing, Zentralblatt für die gesamte Therapie 1913, No. 7, p. 337.

Stümpke, Münchener medizinische Wochenschrift 1913, No. 27, p. 1489.

Bäumer, Deutsche medizinische Wochenschrift 1913, No. 28, p. 1361.

* Compare Merck's Report 1911 and 1912.

slight coryza or mild disturbance of the gastro-intestinal tract the author frequently continued the administration of iodostarin and found that this may be done without difficulty. If necessary, the doses may be decreased. Stümpke does not consider it advisable to exceed a daily dose of six tablets, as this amount represents the attainable limit of action and is free from the dangers attending the use of too large doses. At the commencement of treatment not more than two or three tablets should be given daily. Bäumer obtained similar results.

Rabajoli and Th. Pertik prescribed iodostarin in pulmonary tuberculosis. Rabajoli found that the preparation is quickly absorbed and consequently small amounts of iodine are demonstrable in the urine and saliva already after thirty-five to forty minutes. It is excreted much more slowly than the alkaline iodides. In no case did he observe symptoms of iodism, on the contrary, he obtained uniformly good results inasmuch as the general condition improved and there was a gain in weight. Pertik confirms the tolerance of the preparation, provided not more than three tablets are taken daily. He also ascribes to it a good effect upon the heart's action and respiration. In addition to the improvement of the general condition and of the appetite this medication leads to a decrease in the expectoration and in the number of tubercle bacilli in the sputum. Hæmoptysis occurred in two cases only (in an advanced stage), and the author is unable to state whether this was due to the iodostarin.

Since iodostarin passes through the stomach unchanged and is quickly absorbed in the intestine, M. Galazer used it to determine the motility of the stomach. His investigations show that a conclusion may be drawn regarding the presence of anatomical changes from the rapidity with which iodine appears in the saliva. The result of this test is not influenced by the gastric secretion.

Ipecacuanha.

H. G. Beck made use of a new method of administration of ipecacuanha in the treatment of amœbic dysentery. By means of the Einhorn duodenal tube he introduces directly

Rabajoli, *Pensiero medico* 1913, No. 13.

Pertik, *Deutsche medizinische Wochenschrift* 1913, No. 2, p. 75.
Galazer, *Wratschebnaja Gazeta* 1913, No. 21.

Beck, *Journal of the American Medical Association*, Dec. 14, 1912.

into the duodenum one to two drachms (3.5—7 grammes) of powdered ipecacuanha, suspended in mucilage of acacia or macerated in plain warm water. He used this treatment in seven cases, all of which were extremely chronic and refractory, three of them being complicated with liver abscesses, and obtained striking results. He says that large duodenal doses of ipecacuanha seem to have no injurious effects. There are occasionally gastro-intestinal symptoms such as nausea, vomiting and diarrhoea; also slight general depression may appear with a tendency to lowering of the blood pressure. In the treatment by duodenal administration according to Beck's method the above mentioned suspension of the powdered root may be replaced by a solution containing 0.08 to 0.16 gramme ($1\frac{1}{4}$ — $2\frac{1}{2}$ grains) of emetine hydrochloride*.

The successes obtained in the treatment of amoebic dysentery with hepatitis by ipecacuanha induced T. H. Delany to try the effect of this drug in cholelithiasis. Among other cases he gave to a woman, aged 50, with severe gall-stone colic and jaundice in whom an operation could not be performed, injections of morphine and every four hours a dose of 0.06 gramme (1 grain) of Dover's powder and 0.06 gramme (1 grain) of powdered ipecacuanha and gradually increased the doses so that by the tenth day the patient was taking 1 gramme (16 grains) of powdered ipecacuanha and 0.5 gramme (8 grains) of Dover's powder within the twenty-four hours. At the end of thirteen days the jaundice was much less and the pain was considerably relieved; after the twenty-first day the enlargement of the gall-bladder had considerably subsided, after four weeks the intestinal functions had become normal, and at the end of thirty-five days the gall-bladder could no longer be palpated and the jaundice had disappeared. No recurrence took place. The author achieved similar successes in other cases of gall-stone disease. He points out that the drug is vomited at first in most cases, but this can usually be arrested by the opium administered at the same time; should this not be the case recourse may be had to subcutaneous injections of emetine hydrochloride.

A new preparation made from Rio ipecacuanha has been placed on the market under the name of "riopan". It is a

* Compare the article on Emetine, page 200.

Delany, Indian Medical Gazette 1913, No. 5, p. 180.

brownish powder, readily soluble in water. According to E. Grabs, the hydrochlorides of the ipecacuanha alkaloids constitute 50 p.c. of the preparation, in addition to which it also contains the other active principles of the root (ipecacuanhic acid). Administered in the form of drops (0.05:10), it did not act well as an expectorant and readily gave rise to vomiting, wherefore the author abandoned this mode of administration. Nor did its administration in the form of tablets give satisfaction, since they caused rawness in the throat. According to Grabs the best method of administration of the preparation is in the form of a mixture, or of tablets prepared with tragacanth. The author recommends the following mixture:

Rp. Riopan 0.025 gramme ($\frac{2}{5}$ grain)

Aq. dest. 150 grammes (5 oz)

Syrup. 20 „ ($\frac{1}{2}$ oz)

M. Sig.: 3 to 5 tablespoonfuls to be taken daily.

The tablets contain 2.25 milligrammes of riopan, so that each tablet is equivalent to one tablespoonful of an infusion of ipecacuanha 1 in 150. The addition of tragacanth prevents the feeling of rawness in the throat. The tablets should not be chewed or swallowed whole, but should be sucked. They are intended for use as an expectorant in the treatment of bronchitis, congestive and chronic bronchitis, and pulmonary tuberculosis.

Ipecacuanha, Tincture of

The use of tincture of ipecacuanha as an astringent in diarrhoea is well known*, and recently Rousseau-Saint-Philippe has recommended it for the treatment of obstinate disturbances of digestion in children. These affections with their secondary troubles such as constipation, loss of appetite, intestinal atony, aepsia and dyspepsia, which in turn give rise to anæmia, wasting, intoxications, etc., in the author's opinion form an almost uniform type of disease which is specially characterized by the occasional secretion of mucous substances containing membranes. Drugs, such as antiseptics, are mostly useless, or effect only temporary improvement.

Grabs, Deutsche medizinische Wochenschrift 1913, No. 44, p. 2146.

* Compare Merck's Index 1910, p. 256.

Rousseau-Saint-Philippe, Journal de médecine de Bordeaux 1913, No. 14. — Deutsche Medizinalzeitung 1913, No. 31, p. 522.

The symptoms referable to deficient function of the liver and bile can be removed by the use of tincture of ipecacuanha. At first small doses (one drop) are given in a little sugar and water, twice a day, half an hour to one hour before meals, and according to the age of child (six months to four years and over) the dose is increased daily by one drop until a dose of 5 to 20 drops is reached. At the same time a varied diet is given, e. g., milk and farinaceous foods (with the addition of maltose), and later finely minced mutton. The treatment must be continued for some time if it is to prove successful.

Iridium Chloride.

As a test for nitric acid in the presence of nitrous acid, W. N. Iwanow suggests the use of a solution of tetravalent salts of iridium, iridium oxide (IrO_2), or of iridium and ammonium chloride ($\text{Ir}[\text{NH}_2]_2 \text{Cl}_6$) in sulphuric acid. Iridium chloride (IrCl_3), or iridium and potassium chloride ($\text{IrK}_2 \text{Cl}_6$), may also be used for the same purpose. Iridium chloride is readily soluble in water, while iridium and potassium chloride is more soluble in hot water. Both salts yield reddish-brown solutions.

The reagent is prepared in the following manner: 0.025 gramme of iridium chloride, or of iridium and potassium chloride, is dissolved in 3—5 c.c. of water and 100 c.c. of concentrated sulphuric acid (98—99 p.c.) are added, with constant stirring, whereupon the mixture is heated to boiling. The colour now changes from pink to violet, then to yellow and finally the mixture becomes colourless. The colourless reagent must be kept in well-stoppered bottles. The finished reagent should have a content of 96—96.5 p.c. of $\text{H}_2 \text{SO}_4$, therefore the proportions given above must be rigidly adhered to, otherwise the reagent is useless. To apply the test, 5 c.c. of the reagent are heated in a suitable test-tube to boiling, whereupon the substance to be tested is added in a solid form. Liquids to be tested must therefore first be evaporated to dryness with the addition of a slight excess of solution of sodium hydroxide. The reagent is not heated while the substance is being added. Nitric acid in amounts of 0.0001—0.0005 gramme produces a transient blue coloration, if more than 0.0005 to 0.001 gramme

is present the colour is permanent. Nitrous acid even in large amounts causes only a greenish-yellow coloration. To prevent the conversion of nitrous acid into nitric acid by the steam* the test is best carried out in a current of carbon dioxide which carries away the steam which is formed.

Iron, Colloidal

After it had been found that the subcutaneous exhibition of colloidal iron prepared by chemical means was too painful, B. G. Duhamel and G. Rebière undertook the pharmacological study of so-called "electromartiol", an electrically prepared form of colloidal iron. The authors state that the preparation occurs as an amber-coloured liquid which contains 0.05 p.c. of iron. It can be injected subcutaneously, intramuscularly or intravenously without causing pain. It is apparently harmless in other respects as well, for even in fourfold concentration and with the prolonged use of large doses in rabbits no injurious effect on the kidneys, liver or spleen was observed. The action of the preparation on the blood manifests itself by a considerable increase in the number of red blood corpuscles, which is said to take place more rapidly than following the use of iron citrate. In addition to its iron action this new remedy should possess a certain pharmacological value by reason of its colloidal nature; however, its therapeutic use awaits investigation.

Iron Oxide.

Ferroso-ferric oxide, $\text{Fe}_3\text{O}_4 \cdot \text{H}_2\text{O}$, a black powder soluble in hydrochloric acid, has been employed by H. Spude for the treatment of cancer.

Spude bases his method upon the observation that arsenic is more injurious to the less resistant cancer cells than to the epithelial cells which are biologically closely related to the cancer cells, whereby a direct as well as indirect influence may be displayed. The indirect influence leads to the display of a toxic action which paralyses and damages the capillaries, and thus causes a maximum degree of hyperæmia and of fibrinous transudation. It occurred to the author that it might

* $\text{N}_2\text{O}_4 + \text{H}_2\text{O} = \text{HNO}_3 + \text{HNO}_2$.

Duhamel-Rebière, *Presse médicale* 1913, No. 14, p. 133.

Spude, *Münchener medizinische Wochenschrift* 1912, No. 31, p. 1713;

Zeitschrift für Krebsforschung 1913, Vol. 13, No. 1, p. 139.

be possible to produce, or to increase, the hyperæmia and transudation caused by the injurious action of arsenic on the epithelial or cancer cells by a mechanical irritation of the vascular cells, which, while capable of causing alterations would be of a transient nature and consequently would increase the direct action of arsenic on the cancer cells. He attempted to achieve this by infiltrating the tumour and its immediate neighbourhood with an extremely fine-grained preparation of magnetic iron and then causing an alternating current magnet to act upon these fine grains of iron. The magnetic material was thereby caused to vibrate, with the result that the vessels were irritated, or enlarged and altered, and ultimately transudation occurred. The action of the alternating current magnet on the tumour impregnated by puncture with ferroso-ferric oxide proved in itself to be a healing factor, while the effect was further greatly enhanced by combining this treatment with injections of atoxyl, i. e., one intravenous injection of 0.1 to 0.2 gramme ($1\frac{1}{2}$ —3 grains) every four to eight days. Basing on a few successes, Spude hopes that this "electromagnetic and arsenic irritant treatment" may prove useful also in inoperable and recurring carcinomata of internal organs, although in this case the method of application and technique would have to be considerably modified.

Iron Perchloride.

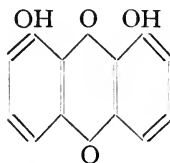
J. H. Garrett states that a concentrated solution of ferric chloride is a good remedy for treating ringworm of the scalp (herpes tonsure). For the treatment of school children the author employed the *Liquor Ferri Perchloridi Fortis* of the British Pharmacopœia 1898, which has a specific gravity of 1.42 and contains 22.5 grammes of iron in 100 c. c. (110 minims contain $22\frac{1}{2}$ grains) = 15.84 grammes of iron in 100 grammes, or 46 p. c. of ferric chloride.

The strong perchloride solution is dabbed on the scalp with a camel-hair brush until the scalp is thoroughly stained with it. The patches affected are treated every second day for three times, afterwards every third day for six times, when a cure will generally be effected. Before the application of the perchloride of iron is begun the scalp should be freed from grease by the use of petroleum ether and the

head is given a good wash. However, the head should not afterwards be often washed during the treatment. By holding the hair aside the solution can be made to stain the scalp thoroughly without cutting the hair, although it is well to cut the hair close over the affected patches. The parts unaffected with ringworm may be protected by a suitable dressing. Under the action of the ferric chloride a scurf is formed which comes away from the scalp in the course of some days, leaving a healthy skin beneath. This treatment has the advantage that the children are not prevented from going to school, as the risk of infection appears to be removed after treatment with iron perchloride. It may be mentioned that Garrett states that the use of dilute solutions does not appear to be so successful, at least he was unable to obtain the same results when using the weaker preparation, i. e., the *Liquor Ferri Perchloridi* of the *British Pharmacopœia*. Hence it is essential to use the strong solution, although it may occasionally cause an inflammatory reaction.

Istizin.

Istizin is the name applied to 1,8 dioxyanthraquinone. It occurs as an orange-yellow crystalline, odourless and tasteless powder. Melting point 190° — 192° C. It has the chemical formula:



It dissolves with difficulty in water and in the ordinary organic solvents, and also in alkalis with which it yields a cherry-red solution.

The pharmacological (purgative) action of istizin is based upon its chemical relationship to emodin, which occurs either free or in combination in some well-known drugs such as aloes, rhubarb, senna and buckthorn. Emodin differs from istizin only in that it contains another $\text{CH}_2 \cdot \text{OH}$ group. Apart from its purgative effect, istizin possesses no further pharmacological action. Since a small part of the drug is absorbed the urine assumes a reddish colour after taking istizin. The amounts absorbed are, however, so small that according to

E. Ebstein irritation of the kidneys need not be feared. After this author had definitely established the purgative action of this drug by experiments on animals he undertook its clinical investigation. He made use of tablets containing 0.3 gramme (5 grains) of istizin, and prescribed half to one and a half tablets per os, i. e., doses of 0.15 to 0.45 gramme ($2\frac{1}{3}$ —7 grains). It is advisable to take the tablets in water in which they are allowed to disintegrate, so that the drug reaches the stomach in as fine a state of subdivision as possible. If the above cited dose is administered at night, about an hour and a half after the evening meal, a pultaceous and formed evacuation may be reckoned upon within from ten to fourteen hours; thin stools or explosive-like defæcation were never observed. On the other hand, the author states that after a dose of 0.3 gramme (5 grains), and especially after 0.45 gramme (7 grains), as a rule two, and sometimes three or four, evacuations follow. In some cases the patients complain of slight griping pain, which is seldom troublesome or inconvenient; on the other hand, pains in the region of the kidneys were never observed.

Ebstein was able to demonstrate by Röntgenological examinations that after evacuation by istizin the gastro-intestinal tract is almost completely emptied, and further that the laxative action after doses of 0.3 and 0.45 gramme (5 and 7 grains) sets in only after twelve hours.

According to Ebstein, istizin is indicated in mild as well as severe forms of constipation, both atonic and spastic. It appears to be specially indicated in bedridden patients and in patients who have to lie in bed. In very obstinate cases of habitual constipation it may be used with good results when large amounts of oil are given rectally to lubricate the bowel.

Kalzine.

In an exceptionally severe case of urticaria in childbed K. Bollag obtained a noteworthy success by the use of kalzine*. The patient, a woman aged 31, who was otherwise healthy, developed itching and smarting over the whole body

Ebstein, Medizinische Klinik 1913, No. 18, p. 708.

Bollag, Münchener medizinische Wochenschrift 1913, No. 45, p. 2514.

* Compare Merck's Report 1912, p. 427 and the article on Calcium Chloride in this Report, p. 132.

a few days after parturition and showed an urticarial eruption which extended from the legs and thighs and covered the whole body. On the third day the patient was given an injection of kalzine, which was made as directed into the upper quadrant of the gluteal region. On the following morning the patient appeared much brighter and with the exception of the hands, arms and feet, the urticarial eruption had quite disappeared; according to Bollag this result was directly due to the kalzine. Two days later, as a prophylactic measure and to remove the œdema of the hands still present, the contents of another ampoule of kalzine were injected into the other thigh. As after the first injection, the site of injection showed no reaction, but remained sensitive during the day. The further progress of the puerperium was favourable and afebrile. The author is unable to offer an explanation for the occurrence of the severe rash, nevertheless the successful result obtained justifies the use of kalzine in similar cases.

Kaolin, Sterilized

R. Burmeister states that when using rubber gloves during operations the employment of sterilized kaolin offers several advantages. He adopts the following procedure: After sterilizing the gloves in the usual way they are placed in sterile water or in solution of mercuric chloride, and the hands are also disinfected as usual. Thereupon the hands are rubbed with sterile water and kaolin until they are covered with a coating of kaolin paste, over which the wet gloves can be easily drawn. The gloves are cleansed with sterile water to remove the kaolin paste deposited on the outside of the gloves while drawing them on. The gloves now fit closely without any air or water bubbles, and, according to the author, the operation is performed with much greater comfort than without the use of kaolin. Further, after the operation the gloves can be removed without difficulty so that in the majority of cases they are not damaged. In addition, with this method the hands are protected and under the coating of kaolin they are not macerated to the same extent as is the case without its use. Hence the advantages of using kaolin in the gloves consist in being able to draw the gloves on and off

with greater ease, protection of the hands, while the gloves fit well and a saving in gloves is effected.

Günther describes a similar procedure with this difference that he applies the kaolin by means of alcohol to the hands, which are wiped one minute afterwards, so that only a fine layer of kaolin remains. In addition to greater ease in drawing on the gloves Günther observed that the hands showed less tendency to sweat, which is a further advantage of this method. On the other hand, he states that the operator's skin becomes rough and sore, therefore he does not recommend the use of his method. Burmeister ascribes Günther's failures to the use of alcohol, and he states he has used his own method for over a year with satisfactory results and without experiencing any inconvenience.

Kutscher discusses the value of Liermann's method of disinfecting the hands with Liermann's paste*, which has been confirmed by the investigations of Küster and Geisse. He does not endorse the favourable opinion expressed of Liermann's method, and states that it is in no way superior to washing with alcohol alone.

Kaolin is of special importance in the treatment of leucorrhœa, in which dry treatment with kaolin** yields excellent results. This is confirmed by E. Puppel, whose experience induces him to state that irrigations in leucorrhœa in young girls should be avoided. In cases in which local treatment is indicated he introduces a thin opaque glass speculum or a urethral dilator, wipes out the vagina and insufflates kaolin by means of an insufflator. If the hymenal ring is too narrow the insufflator can be introduced without a speculum. The author does not prescribe irrigations, but daily washings or sitz-baths. In leucorrhœa during pregnancy, which is not due to a specific bacterial infection, but is caused by hyperæmia of the mucous membranes, the author uses only sterilized kaolin which he introduces through a speculum, keeping it in place by a plug. The treatment of gonorrhœa requires a consid-

Günther, *ibidem* 1913, No. 13, p. 461.

Burmeister, *ibidem* 1913, No. 29, p. 1141.

* Compare Merck's Report 1911, p. 427.

Küster-Geisse, Merck's Report 1912, p. 430.

Kutscher, *Berliner klinische Wochenschrift* 1913, No. 14, p. 629.

** Compare my former Reports.

Puppel, *Fortschritte der Medizin* 1913, No. 26, p. 714.

erable amount of patience, and Puppel demands that the dry treatment with kaolin should be carried out by the doctor, and not entrusted to the patient.

Since kaolin is quite inert it deserves special attention in the care of the teeth. According to Küster and Weisbach the use of kaolin as a tooth powder yields the same results as the best specialities for the care of the mouth and teeth at present in the market.

P. G. Unna reports on the use of kaolin in dermatological work. For details his interesting paper should be consulted, as it does not lend itself to brief abstraction.

Lactophenin.

M. Peltzer records some observations on lactophenin, which is extensively used as an antipyretic, antineuralgic, hypnotic and sedative and which enjoys a high reputation in medicine*. An observation which he made upon himself is of special interest. After prolonged bromine medication he wished to effect the gradual withdrawal of bromine, but was unable to do so until he took lactophenin in doses of 1 gramme (15 grains). He succeeded not only in cutting off completely the use of bromine, but later was able to do without lactophenin as well. Further, the author reports a case in which lactophenin was taken for the same purpose without the practitioner's knowledge for a prolonged period (108 days) every night, whereupon attacks of dizziness occurred, which Peltzer does not ascribe to the lactophenin alone but also to the phenacetin taken at the same time. After stopping the lactophenin, and by drinking large amounts of water, in addition to plenty of fresh air and the use of mild laxatives the attacks of dizziness disappeared in the course of a fortnight. Basing on this experience and on the statements in the literature, the author comes to the following conclusions:

Lactophenin (lactylphenetidin), according to Poulsson the best of the compounds prepared after the example of phenacetin, is not quite free from secondary effects even in those cases in which it is given as a reliable antipyretic, although

Küster-Weisbach, *Deutsche Monatsschrift für Zahnheilkunde* 1913, No. 2, p. 123.

Unna, *Medizinische Klinik* 1913, No. 41, p. 1675 and No. 42, p. 1725.

Peltzer, *Fortschritte der Medizin* 1913, No. 6, p. 155.

* Compare Merck's Report 1894, p. 74.

manifestations of this kind (collapse, cyanosis, arrhythmia of the pulse, rashes, etc.) are a very rare occurrence. The secondary effects most frequently mentioned are sweating and rigor. If the cases of typhoid reported in the literature by a few authors are compared with the cases in which the occurrence of secondary effects is reported, it will be seen, according to Peltzer, that unwelcome secondary effects occur in about one case in a hundred, but in reality such cases are doubtless much rarer.

When using the drug as an antineuralgic collapse was observed in one case only, in which the patient took 2 grammes (30 grains) at one dose on an empty stomach.

When prescribing lactophenin care should be taken that it is not given for too long a period without interruption, as otherwise it may display a cumulative action, as in the above cited case of misuse of lactophenin. Peltzer suggests giving it as a hypnotic to afebrile patients in doses of 0.5 to 1 gramme ($7\frac{1}{2}$ —15 grains) for not more than eight or ten days, and then to allow an interval or prescribe another drug, until the phenols have been eliminated. If necessary the elimination of the drug can be hastened by increasing diuresis. Further, intolerance or idiosyncrasy to lactophenin may be met with, at least the author observed in one case that a dose of 0.5 gramme ($7\frac{1}{2}$ grains) caused dizziness.

In a further communication Peltzer draws attention to the advantages of lactophenin when properly administered, i. e., not continuously. Given in doses of 0.5 to 1 gramme in cases of mild and moderate insomnia it is the only drug which, in his experience, leaves the head absolutely free on the following day, in most cases it even leaves a certain degree of euphoria behind.

Larosan.

Under this designation a casein-calcium is issued with a content of 2.5 p. c. of CaO. It occurs as a fine, bulky, tasteless and odourless white powder; its aqueous solution has an alkaline reaction. According to Stöltzner and Forcart it

Peltzer, *Fortschritte der Medizin* 1913, No. 19, p. 523.

Stöltzner, *Münchener medizinische Wochenschrift* 1913, No. 6, p. 291 and *Medizinische Klinik* 1913, No. 22, p. 868.

Forcart, *Münchener medizinische Wochenschrift* 1913, No. 22, p. 1199.

is employed as a dietetic remedy in disturbances of nutrition and in diarrhoeas, particularly in sucklings and children. In the form of a solution prepared with diluted milk it possesses the therapeutic properties of albumin milk. To prepare laroson milk 20 grammes ($\frac{2}{3}$ oz) of laroson are mixed with about 150 c. c. (5 oz) of fresh milk whereupon about 350 c. c. (12 oz) of milk are added and the whole is boiled for a few minutes. According to Stöltzner, laroson is especially indicated in all disturbances of nutrition; of course, in enteral and parenteral infections a striking success cannot be expected, any more than is the case with other dietetic preparations, for instance, albumin milk. Forcart obtained uniformly good results with laroson milk in sucklings suffering from gastro-intestinal affections. He states that sugar may be added to raise the calories. As a diluent he usually employs oatmeal water, and sometimes pap made of flour. The value of laroson milk is confirmed by Ph. Wehner, J. Stawsky and Vigener.

Lecithin.

In succession to my monograph on lecithin* mention may be briefly made of some of the more important papers published during the past year.

D. M. Lawrow discusses the influence of lecithin upon drugs, to which H. de Waele first drew attention. For his experiments he used frogs in which ricin and lecithin were injected subcutaneously in order to study the effect of lecithin on the action of ricin. He found that doses of 0.0015 to 0.003 gramme of lecithin markedly increase the action of ricin, while larger doses increase the ricin action during the first ten or eleven days, afterwards, however, they mitigate its action. The effect of lecithin manifested itself best in frogs which had not hibernated. In collaboration with W. Woronzow the author demonstrated by experiments on animals that lecithin has an analeptic action in disturbances of circulation caused by alcohol, chloral

Wehner, Deutsche medizinische Wochenschrift 1913, No. 44, p. 2147.

Stawsky, Therapeutisches Obshrenie 1913, No. 18.

Vigener, Berliner klinische Wochenschrift 1913, No. 48, p. 2257.

* Merck's Wissenschaftliche Abhandlungen No. 9 or Merck's Report 1912, p. 1—71.

Lawrow, Biochemische Zeitschrift 1913, Vol. 54, p. 16.

Lawrow-Woronzow, Archives internationales de pharmacodynamie et de thérapie 1912, Vol. 22, p. 392.

hydrate, etc. By the intravenous injection of as little as 0.05 gramme of lecithin in the form of an emulsion the action of the heart can be strengthened and accelerated to such an extent that the blood pressure, even if extremely low, begins to rise. In the same way the injurious effect of muscarine on the circulation is partly abolished by lecithin.

E. Hanschmidt undertook experiments on rabbits, guinea-pigs, dogs and mice to elucidate the action of lecithin in poisoning by various drugs. His experiments show that lecithin, when introduced into a normal animal organism, displays no toxic effect, in fact very large doses of lecithin may be injected subcutaneously, intravenously or intraperitoneally without danger. It displays a distinct action on various poisons, but this action varies and is influenced by the pharmacodynamic effect of the poison, the amount employed, and by the condition of the organism, or rather its content of lipoids. In cases of poisoning by curare, strychnine, ethyl alcohol, chloral hydrate, veronal-sodium, and morphine, lecithin uniformly inhibited the toxic effect. On the other hand, lecithin appears to enhance the action of some poisons (ricin).

The absorption of lecithin in the gastro-intestinal tract is discussed by R. Ehrmann and H. Kruspe. Whereas hitherto it had generally been accepted, in accordance with the investigations of Kutscher, Lohmann and Bokay, that lecithin is possibly split up by the pancreatic juice and absorbed in the form of glycerophosphoric acid, choline and fatty acids, Ehrmann found that also the secretion of bile plays an important part in the absorption of lecithin. Ehrmann assumes that bile is capable of dissolving lecithin, so that it is absorbed unchanged in the form of a solution (in bile).

Calcaterra studied the action of lecithin on diphtheria, typhoid and tubercle bacilli, and found that the addition of small amounts of lecithin to the nutrient media promotes the development of these pathogenic germs, whereas larger amounts

Hanschmidt, *Biochemische Zeitschrift* 1913, Vol. 51, p. 171.

Ehrmann - Kruspe, *Berliner klinische Wochenschrift* 1913, No. 24, p. 1111.

Kutscher - Lohmann, *Zeitschrift für physiologische Chemie* 1903, Vol. 39, p. 159 and 313.

Bokay, *ibidem* 1877/78, Vol. 1, p. 157.

Calcaterra, *Annali dell'Istituto Maragliano*, Vol. 6, No. 6. — *Zentralblatt für innere Medizin* 1913, No. 29, p. 746.

cause bacteriolysis. Indeed, he found that a solution of typhoid bacilli effected by means of lecithin is capable of producing antibodies in the animal body and of rendering animals immune. Lecithin is also credited with the property of preventing the manifestations of anaphylaxis which occur as a result of immunisation by serum.

The results of investigations undertaken by T. Brailsford-Robertson and Th. C. Burnett possess a certain amount of therapeutic interest. The authors were able to demonstrate that intratumoral injections of lecithin in Flexner-Jobling's rat carcinoma retard the growth of metastases, or are even capable of preventing the formation of metastases. The primary tumour is also beneficially influenced by these injections.

The investigations of C. Neuberg and L. Karczag have a certain importance for the biological action of radiotherapy. Whereas Schwarz and others had found that the hæmolysis of the red blood corpuscles under the action of radium is due to the cleavage of the lecithin they contain, both authors established that no definite proof could be adduced in support of a cleavage of lecithin by radio-active substances.

J. Nerking deals with the therapeutic value of lecithin. He states that lecithin has now found a permanent place in materia medica as an internal remedy in a number of affections, especially in nervous conditions of exhaustion, diseases of the blood and cachectic processes. On the other hand, but little attention has been paid to its subcutaneous injection, although in view of the well-known tonic effect of pure lecithin injections of lecithin should prove particularly effective in severe cases. However, the author again emphasises* the necessity of using a carefully prepared and extremely pure lecithin to obtain a successful result. Lecithalbumins, i. e., preparations consisting principally of dried and powdered egg yolk freed from fat, such as are contained in several products extensively advertised as "purest lecithin", or "physiologically pure lecithin", are stated to be of little value even when given by mouth. Lecithin of

Robertson-Burnett, *Journal of Experimental Medicine* 1913, Vol. 17, p. 344.

Neuberg-Karczag, *Radium in Biologie und Heilkunde* 1913, Vol. 2, p. 116.

Nerking, *Zentralblatt für die gesamte Therapie* 1913, No. 2, p. 58.

* Compare Merck's Report 1912, p. 36.

the highest chemical purity alone is able to display a peculiar, beneficial effect, and for subcutaneous injection the use of a preparation answering this description is essential, since under certain circumstances an impure preparation may even prove harmful and dangerous. Hitherto solutions of lecithin in olive oil have generally been used for subcutaneous injection; however, an aqueous emulsion of lecithin prepared with physiological salt solution offers the great advantage that it can be injected not only subcutaneously, but also intravenously and intramuscularly. Nerking states that his proposal to inject subcutaneously lecithin emulsion after anæsthesia deserves wider recognition since it has yielded excellent results*. Further, the subcutaneous injection of lecithin emulsion is useful in epilepsy, if this treatment is continued for some time, and also in severe nervous conditions, sexual neurasthenia, impotence, leukæmia and anæmias. The author has also tried it in arteriosclerosis and gout, since lecithin apparently prevents the deposit of lime in the tissues and dissolves the lime already present. He suggests undertaking similar experiments since the injections are harmless; so far he has been unable to form a definite opinion as to their value. The treatment consists in injecting under the skin of the back 2 or 5 c.c., according to the severity of the case, of the lecithin emulsion supplied by me. Of course, the injection must be made under aseptic precautions, otherwise symptoms of irritation may occur.

Analytical methods of testing lecithin have been published by R. Cohn; for details the original paper should be consulted.

Lenicet.

For the treatment of discharges from the female genitals G. Katz employed a combination of lenicet** with kaolin and

* The use of lecithin after anæsthesia is all the more justified since L. Hess and R. von Frisch found a phosphorus-containing lipid (i. e., a lecithin) after prolonged anæsthesia in the urine of women suffering from gynæcological affections. This finding shows that breaking down of lipoids takes place in the nervous system during narcosis. (*Wiener klinische Wochenschrift* 1913, No. 8, p. 290.)

Cohn, *Zeitschrift für öffentliche Chemie* 1913, No. 3, p. 54. —

Chemiker-Zeitung 1913, No. 57, p. 581 and No. 98, p. 985.

Katz, *Berliner klinische Wochenschrift* 1913, No. 17, p. 781.

** Compare Merck's Reports 1905—1911.

peroxides, or with silver acetate, which yielded excellent results in his hands. After cleansing the vagina with cotton wool two or three teaspoonfuls of the powder are introduced by means of a speculum, and the powder is distributed in such a way as to protect the vaginal mucous membrane from the secretion coming from the cervix. The powder is allowed to remain until the following day, when irrigation with lukewarm chamomile infusion is performed prior to again introducing the powder; the irrigation is designed to remove the powder impregnated with the discharge and thrown off epithelium. The author adopted this treatment in cases of acute and chronic gonorrhœa, erosions of gonorrhœal and non-gonorrhœal origin, catarrh of the cervix, and in all forms of colpitis and vulvitis, using alternately a mixture of lenicet, kaolin and peroxide, and a mixture of lenicet, kaolin and silver acetate.

In veterinary practice Stietenroth recommends the use of lenicet as a dusting powder (lenicet 20 parts, kaolin and talc, of each 40 parts), and as a 5 to 10 p.c. ointment. He used the dusting powder in the treatment of wounds, ulcers of the coronet and claws, contagious vaginal catarrh and earwigs in dogs. He found lenicet especially useful in inflammation of the external ear in dogs. In these cases the auricle of the animal is cleansed every second or fourth day with a 3 p.c. solution of resorcin in alcohol, and after drying with cotton wool 20 p.c. lenicet powder is applied. Even old-standing cases are said to be cured by this treatment within a short time. The foul smell of the discharge disappears, and the secretion usually ceases completely after a short time.

The author has used lenicet dusting powder, mixed with sufficient water to form a paste, with successful results in the treatment of burns and contusions, and also in severe forms of malanders. In the form of an ointment he used lenicet in wounds, phlegmons, inflammation of the prepuce and phimosis, eczemas, dermatitis, mild inflammations of the udder, etc. It always yielded good results and displayed in particular an analgesic, or antipruritic effect. The ointment also proved useful in various eye diseases such as conjunctivitis, keratitis, ulcer of the cornea, etc.

Leptynol.

Using the fact that the metals of the platinum group are excellent catalysts as a basis, M. Kauffmann undertook experiments with the hydrosols and hydroxides of palladium, platinum, rhodium, iridium, ruthenium and osmium with a view to ascertaining whether these substances might be used therapeutically as oxygen-carriers in the general disturbance of oxidation in obesity. The positive results of his trials induced him to use palladous hydroxide, the colloidal solution of which in wool fat and liquid paraffin (leptynol) can be injected subcutaneously. The preparation is issued with a content of 2.5 p.c. of palladium in the form of $\text{Pd}(\text{OH})_2$, so that 1 c.c. is equivalent to 25 milligrammes of palladium; it is somewhat viscid and should be warmed before injecting. According to Kauffmann's directions 2 c.c. are injected deep into the abdominal fat, and on the following days the patients are made to take as much exercise as possible. The best results are obtained by a combination of treatment by metal and a Marienbad diet cure. The author's favourable results induced W. Gorn to make a study of Kauffmann's method.

In the first place, Gorn draws attention to the fact that the use of leptynol was never followed by any local reaction, nor did he observe any marked disturbance in the general health of his patients. However, in making the injection care should be taken to ensure the preparation being deposited at a depth of at least 2 to 3 cm. ($\frac{4}{5}$ — $1\frac{1}{5}$ in.), as infiltrations or abscesses may occur if it is injected subcutaneously or superficially. In the author's experience severe local symptoms of irritation are always a sign of faulty technique, which therefore requires special care. A further condition which is essential with leptynol treatment is the strict observance of the dietary. As a rule, two injections of 50 to 100 milligrammes of $\text{Pd}(\text{OH})_2$ are made weekly, and this treatment can be carried out without difficulty even in out-patients. In addition, the author prescribed plenty of exercise and milk days according to Moritz's directions — he made his patients drink two litres of milk daily, taken in five portions. The feeling of thirst which occasionally occurs is relieved by small pieces of ice. The

Kauffmann, Münchener medizinische Wochenschrift 1913, No. 10, p. 525 and No. 23, p. 1260.

Gorn, Münchener medizinische Wochenschrift 1913, No. 35, p. 1935.

patients scarcely ever complained of a feeling of hunger. With this treatment the author obtained in three cases, after two injections of 80 and 100 milligrammes of palladous hydroxide, a reduction in weight of 3.7 to 8 kilogrammes in one week. In other cases the loss of weight varied from 3.4 to 2.6 kilogrammes, and in two cases it amounted to only 1.8 kilogrammes. Cases of slight adiposity benefited least of all.

Gorn has also obtained good results with injections of leptynol in various psychoses. Especially akinetic states in hebephrenia and psychasthenia were to a certain extent beneficially influenced. However, the author is unable to express a definite opinion as to its value in these conditions.

Leucofermantin.

As I have already stated in my Reports, camphorated oil is now being used by operators and gynæcologists as a prophylactic and curative agent in peritonitis. However, the results so far obtained are contradictory and it is not possible to express a definite opinion as to the value of camphor in the treatment of infections of the peritoneum. E. Bircher, who had on a former occasion recommended the use of leucofermantin, again had recourse to the latter after he had failed to obtain any specially satisfactory results with camphor treatment. Although camphorated oil is successful in mobilising protective and defensive substances, it is powerless to prevent paralytic or peritoneal ileus, on the contrary, it appears even to favour it, as the author had occasion to observe. On the other hand, leucofermantin has the advantage of complying with both requirements, i. e., it not only mobilises protective and defensive substances, but also neutralises the harmful bodies they contain and which may probably give rise to the ileus. The dangers of peritonitis, according to Bircher, are apparently due to breaking down of tissues, whereby the serous membranes of the intestines are damaged, resulting in paralysis and death. This result is brought about either by the absorption of toxic products causing paralysis, or the general infection is caused by these products. It is not always possible completely to remove these products by drainage, and therefore fresh complications may ensue. Leucofermantin, Bircher states, is the preparation which most effectively coun-

teracts these processes. The author was able to observe the distinctly beneficial influence of leucofermantin in a large number of cases of suppurative appendicitis and incipient peritonitis. His procedure consisted in carefully wiping away the peritoneal exudate, whereupon 50 to 100 c.c. of leucofermantin, previously warmed to 30° C., are poured in. With this treatment severe cases of peritonitis ran a smoother course, healing took place more surely and within a shorter time, and complications, such as ileus and abscesses, became rarer.

V. L. Neumayer is of opinion that antiferment treatment deserves wider recognition from surgeons than has hitherto been the case. His favourable experience of the use of leucofermantin in suppurative processes* induced him to try it in round ulcer of the stomach, i. e., in the pronounced hyperacidity associated with it. He was led to use leucofermantin on the assumption that healing of the ulcer produced by self-digestion of the stomach might be obtained if the cause of the affection, i. e., the action of pepsin, were inhibited by an antiferment. In a case of round ulcer of the stomach which had become worse in spite of rest cure, Leube's diet, sodium bicarbonate and magnesia and in which moderate hæmatemesis was present, he left off the sodium bicarbonate and gave only leucofermantin, 0.5 c.c. (8 min.) three times daily. The heartburn diminished, and after several days' treatment by Leube's diet and nutrient enemata the patient received ambulatory treatment and the use of leucofermantin was continued. About one month later he was able to resume his occupation.

H. Dun reports on the use of leucofermantin in veterinary practice. In a case of complete hydrarthrosis of the right fetlock-joint in a horse, after the operation the author washed out the articular cavity with perhydrol and introduced 40 grammes ($1\frac{1}{3}$ oz) of leucofermantin powder with a view to preventing suppurative inflammation. After about a fortnight, owing to pain and rise of temperature, the wound was drained, cleansed with perhydrol and liquid leucofermantin was injected. In addition a mercuric chloride dressing was applied. Three days later the inflammation in the joint had subsided and

Neumayer, *Mitteilungen des Vereins der Ärzte in Steiermark* 1913, No. 6.

* Compare *Therapeutische Monatshefte* 1911, No. 9.

Dun, *Münchener tierärztliche Wochenschrift* 1913, No. 13.

a quick recovery ensued, so that about a week later the animal could be used for light work.

Lipiodin.

Lipiodin, according to A. Roth, is the ethyl ester of di-iodobrassicinic acid, of the formula $C_{19}H_{39}Cl:ICCOOC_2H_5$. It is a crystalline compound containing 41.06 p.c. of iodine; melting point $37^{\circ}C$.

Roth tried this preparation in eighteen cases of syphilis, after he had established in two persons who were susceptible to iodine that beyond slight coryza it did not cause any other symptoms of iodism. He gave daily two to four tablets of 0.3 gramme (5 grains) of lipiodin and this treatment yielded satisfactory results. Comparatively small doses display the same therapeutic effect as far larger doses of potassium iodide, showing that the preparation is well utilized in the organism.

J. Hochstätter prescribed lipiodin externally in the form of an ointment with good results. He first used it in a case of struma in which he found that the application of a 40 p.c. ointment caused the goitre to become smaller. Thereupon he used a 5 p.c. ointment in a case of favus in a child and was able to effect a speedy cure. Basing on the results of further investigations he advises the use of lipiodin in the following cases:

1. In prostatitis, in the form of suppositories containing 0.3 gramme (5 grains) of lipiodin, one to be introduced morning and evening.
2. In epididymitis, in the form of a 40 p.c. vasogen which is applied to the scrotum once daily and then covered with a gauze dressing.
3. In scrofulous ulcers of the glands, as a 20 to 40 p.c. lipiodin-vasogen.
4. In herpes scroti, in the form of a 40 p.c. vasogen.

Vasogen is especially suited as a vehicle for lipiodin as the latter is soluble in vasogen in all proportions.

The author states that the use of a 40 p.c. lipiodin ointment in a case of arterio-sclerosis led within six to eight days to a fall in blood pressure and at the same time the troubles were alleviated.

A. Dutoit obtained very satisfactory results by giving one to four tablets in toxic and infectious optic neuritis, neuroretinitis and central choroido-retinitis. In every case the drug effected a speedy and lasting improvement in the power of vision, and the same successful effect was also observed in senile macular degeneration.

Lobelia Inflata.

Tincture of lobelia is prescribed in single doses of up to 20 drops and daily doses of up to 60 drops in asthmatic paroxysms. The remedy is especially indicated in chronic bronchial asthma since its active principle, lobeline, according to J. Nerking, on the one hand, has a milder action than atropine in that it paralyses the vagus-endings and relaxes the bronchial muscles and thereby brings about dilatation of the bronchi, and on the other hand, acts as a direct stimulant to the respiratory centre*. Nerking now states that a tincture prepared from the fresh plant is alone effective, since probably the alkaloid undergoes partial decomposition on keeping through fermentation in the leaves. Further, he considers the dosage to be not sufficiently exact and reliable in consequence of the varying content of lobeline, while the tincture displays an unwelcome secondary effect on the gastro-intestinal tract, consisting in anorexia and diarrhoea. He therefore undertook experiments with the quite fresh drug and tried to find substances capable of neutralising this secondary effect. These he found in *Gentiana lutea* and *Erythraea centaurium*. A combination of tincture of lobelia with the above drugs, according to Nerking, acts as an excellent expectorant in chronic asthma with abundant secretion and may be given for a prolonged period without harm. In the place of this tincture he also

Dutoit, Zeitschrift für Augenheilkunde 1913, p. 24.

Nerking, Moderne Medizin 1913, No. 6, p. 129.

* For this reason the alkaloid lobeline, which is obtainable in the form of its sulphate, deserves wider recognition. It has been used with successful results, in daily doses of 0.05 gramme ($\frac{3}{4}$ grain), increasing up to 0.2—0.4 gramme (3—6 grains) for adults, and for children in daily doses of 0.01 to 0.05 gramme ($\frac{1}{6}$ — $\frac{3}{4}$ grain). Compare Merck's Bericht 1889, p. 48. Dreser states that the above mentioned doses are too large if a pure preparation is used, and advises commencing with smaller doses. (Therapeutische Monatshefte 1890, p. 188.)

used "eurespiran tablets", each of which is equivalent to 0.02 gramme ($\frac{1}{3}$ grain) of *Lobelia inflata*. He gave three or four tablets daily and obtained satisfactory results in a large number of cases; comparatively few cases are said to prove refractory to this treatment. It is also effective in children, to whom half the above doses are given.

Luminal and Luminal-Sodium.

The contributions to medical literature dealing with luminal which appeared during the past year are so numerous that I am compelled to summarize the reports of the individual authors. The value of luminal as a hypnotic in general is discussed by R. Noehte, C. Bachem, Lewinsohn, S. Laache, A. Gregor, F. J. Farnell, G. Pernet, F. Dossin, S. Dahlström, E. Blichert and E. Dosio. The hypnotic and sedative action of the preparation, especially in reference to its use in psychiatric practice, is reported upon by M. Vargas, E. Hermann, J. Collantes, L. Daneo and A. Gorrieri, G. Vidoni, T. Saito, E. Ringier,

Noehte, Reichsmedizinalanzeiger 1913, No. 3.

Bachem, Berliner Klinik 1913, No. 299.

Lewinsohn, 4th International Congress on Physiotherapy, Berlin, 1913, March 26—30.

Laache, Über Schlaf und Schlafstörungen, ihre Ursachen und Behandlungen. 1913. Stuttgart: Ferd. Enke.

Gregor, Therapeutische Monatshefte 1913, No. 8.

Farnell, Journal of the American Medical Association 1913, Vol. 61, p. 192.

Pernet, British Medical Journal 1913, II, p. 312.

Dossin, Le Scalpel 1913, No. 36, p. 604.

Dahlström, Tidskrift for den norske laegeforening 1913, No. 8 and 9.

Blichert, Ugeskrift for Laeger 1913, No. 27.

Dosio, Annali di Freniatria e Scienze affini del R. Manicomio di Torino 1913, Vol. 23, No. 1.

Vargas, Medicina de los niños 1913, No. 165, p. 266.

Hermann, Külön lenyomat Békésvarmegye közkorhazának 1912, évi jelentéséből.

Collantes, Archivos de Ginecopatica y Pediatria 1913, No. 19.

Daneo and A. Gorrieri, Note e Riviste di Psichiatria 1913, Vol. 6, No. 3.

Vidoni, ibidem 1913, Vol. 6, No. 1.

Saito, Medizinische Wochenschrift Tokio 1913.

Ringier, Schweizer Rundschau für Medizin 1913, No. 23, p. 948.

E. Hartung, A. Salerni and G. Lomer, and its use in epilepsy is discussed by G. Pellacani, K. Frankhauser, Meldola, G. Bikeles and L. Zbyszewski, J. van Reysschoot and L. de Moor. E. Calderon, A. Pécheux and L. Lotte have prescribed it in hiccough.

Nochte gives an excellent review of a part of the literature on luminal and of the value of luminal as a hypnotic when given by mouth, and of luminal-sodium following its subcutaneous exhibition. At the commencement he advises caution as regards dosage, in order that idiosyncrasy and secondary effects, such as have been observed inter alia by Farnell and Gregor, may be taken into account. Especially with debilitated patients, such as tabetics and tuberculotics, small doses — 0.1 gramme ($1\frac{1}{2}$ grains) — of luminal should be given at first. He states that such patients, if suffering from bronchitis with abundant secretion, are liable to run great risks, for if sleep is too deep the expectoration may be hastened. Repeated doses of 0.1 gramme ($1\frac{1}{2}$ grains), even in excited patients, often succeed in allaying the excitement. The occurrence of rashes, as has been observed inter alia by Pernet, is a sign of intoxication and the further use of the drug should be stopped. In addition to its hypnotic action luminal also possesses a sedative effect which is particularly useful in the treatment of alcoholic delirium, arterio-sclerotic conditions of excitement, epileptic disturbances of all kinds, motor restlessness in chorea and paralysis agitans, and in conditions of fear. Its analgesic effect is particularly manifest in tabes, arterio-sclerosis and spinal pains. According to Nochte

Hartung, Deutsche medizinische Wochenschrift 1913, No. 7.

Salerni, Riforma medica, February 15, 1913.

Lomer, Psychiatrisch-neurologische Wochenschrift 1913, No. 42, p. 505.

Pellacani, Note e Riviste di Psichiatria 1913, Vol. 6, p. 79.

Frankhauser, Zeitschrift für die gesamte Neurologie und Psychiatrie 1913, No. 4.

Meldola, Hamburger Ärzte-Korrespondenz 1913, No. 9, p. 100.

Bikeles and L. Zbyszewski, Neurologisches Zentralblatt 1913, No. 17.

van Reysschoot, Bulletin de la société de médecine mentale de Belgique 1913, No. 168.

de Moor, Bulletin de la Centraal. Kliniek de Gand 1913, August.

Calderon, Merck's Archives 1913, No. 1, p. 25. (Pacific Medical Journal 1912, December.)

Pécheux and L. Lotte, Echo médical du Nord 1913, No. 28.

the coöperation of a sedative and analgesic effect imparts to luminal a certain amount of similarity to the action of alkaloids, and enables it to be occasionally used as a substitute for morphine. For this reason it may be employed with benefit in the treatment of morphinomania.

Although Noehte's results on the whole reflect the findings of the other above cited authors, nevertheless I shall briefly refer to some of the statements contained in their communications.

Thus, Lewinsohn's statement appears to me to be of special importance since he found luminal an effective hypnotic in heart diseases. He was able to combat these successfully with small doses of 0.1 gramme ($1\frac{1}{2}$ grains), without observing any secondary effects. In the author's opinion the specialist for heart diseases is just as much interested in a good soporific as is the psychiatrist.

Whereas the use of luminal in arterio-sclerosis has been deprecated by other authors, Dahlström reports a case of a patient with severe arterio-sclerosis who took nightly on sixty consecutive days 0.3 gramme (5 grains) of luminal without harm. No rashes appeared nor any craving such as occurs after the use of morphine; however, after forty days' use of the drug he noticed that it began to lose its action. Nevertheless, in agreement with other authors, he advises that, as a rule, luminal should not be administered for longer than five to eight consecutive days without an interval, in view of the risks attending the continuous use of all hypnotics.

Luminal also has an anodyne action. Dahlström used it with good results in a woman affected with paralysis agitans who was unable to sleep owing to cystitic pains. Morphine succeeded in allaying the pains, but was powerless to induce sleep. The author sees a further advantage in the fact that luminal, in the form of luminal-sodium, can be injected subcutaneously*. He injected 2 c. c. of a 25 p. c. solution (= 0.5 gramme of luminal-sodium). With this form of exhibition the effect sets in somewhat later than following its oral administration. Dahlström did not observe any local reaction after subcutaneous injection, and only in exceptional cases it gave

* This advantage of luminal, also mentioned by other authors, is not quite correct inasmuch as the corresponding sodium salt of veronal, veronal-sodium, is readily soluble in water and is extensively used for subcutaneous injection.

rise to an insignificant œdema. As has already been pointed out, for subcutaneous injections only freshly prepared solutions should be employed, and the solution should be prepared at ordinary temperature*.

Dosio considers luminal to be the best hypnotic among the numerous soporifics at present on the market. It can be given by mouth, rectally and subcutaneously and has no injurious action on the heart. Further, in cases of extreme excitement it can be combined with scopolamine. For oral administration he gave in most cases 0.1 gramme ($1\frac{1}{2}$ grains), sometimes as much as 0.4 gramme (6 grains). He prefers to administer the drug at 7 p.m., i. e., two hours after the evening meal. For a subcutaneous injection he gave 2 c.c. of a 20 p.c. solution of luminal-sodium, and in cases of extreme excitement scopolamine as well (a corresponding dose of a solution of: luminal-sodium 2 grammes, scopolamine hydrobromide 0.005 gramme, sterile distilled water 8 grammes). The injections are indicated in cases where the patients refuse other modes of administration. Suppositories of luminal-sodium 0.5 gramme, oil of theobroma 1 gramme, were used with good results in patients suffering from gastro-intestinal affections. In contradistinction to Dahlström, Dosio was unable to observe any habituation to the drug even after four weeks' use of luminal.

Salerni, who made a thorough investigation of luminal in mental diseases, was able to confirm Dosio's conclusions. He found that this drug is more active than the other customary hypnotics, but it cannot entirely replace the use of scopolamine. Lomer, too, prescribed luminal in a number of cases of mental disease, and also in paralysis, dementia, melancholia and alcoholic delirium, often with highly beneficial results. However, in five out of sixteen cases he saw secondary effects, such as lassitude, stupor, gastric disturbances and headache. He gave 0.1 to 0.4 gramme ($1\frac{1}{2}$ —6 grains). As he observed slight cardiac irritation in an alcoholic he considers it advisable to examine the heart before administering the drug. Saito urges caution when using luminal in diseases of the heart and kidneys, otherwise he has come to the conclusion that luminal is an extremely reliable hypnotic when given by mouth, even in small doses. The other above cited psychiatrists

* Compare Merck's Report 1912, p. 259 and 262.

also express a favourable opinion of the value of luminal. Mention may be still be made of Hartung's results:

In cases of simple or moderate sleeplessness doses of 0.1 to 0.3 gramme ($1\frac{1}{2}$ —5 grains) are sufficient for men and women. The author gained the impression that luminal is about $2\frac{1}{2}$ to 3 times more active than veronal. In the conditions of excitement in mania and schizophrenia it is advisable to begin with larger doses (0.5 to 0.7 gramme [$7\frac{1}{2}$ —11 grains]), and as soon as the action has set in to administer 0.3 gramme (5 grains), or less. The drug failed only in one case of schizophrenia, in which scopolamine also proved ineffective. On the other hand, it proved very useful in two cases of hysteria and in one case of epilepsy. Hartung never saw any injurious side-effects, with the exception of drowsiness in two cases. He does not consider this an unwelcome appearance, on the contrary, he regards it as useful since in the treatment of the insane it is sought to bring about a state of insensibility and therefore an after-effect of the above description does not constitute a drawback. Otherwise, in general practice in which this after-effect is not desired, veronal should be preferred since it displays no subsequent effect. In mentally sound persons luminal in doses of 0.05 to 0.1 gramme ($\frac{3}{4}$ — $1\frac{1}{2}$ grains) is equal to veronal as a hypnotic. In consequence of its more powerful action the use of luminal is to be preferred in asylum practice.

In epilepsy, luminal, or luminal-sodium, deserves special consideration among the soporifics used in this malady. Its action is based upon the fact that hypnotics such as chloral hydrate, amylene hydrate, dormiol, veronal, luminal, adalin and bromural, prevent in a striking manner the development of epileptic fits in consequence of irritation of the cortex of the brain. Bikeles lays stress upon the fact that he succeeded in demonstrating pharmacologically this effect, even with small doses which would be insufficient to induce sleep. Hence luminal would appear indicated as a substitute for preparations of bromine in those cases in which a prompt action is desired.

J. van Reysschoot even maintains that luminal is the best anti-epileptic now available. He states that the effective dose is 0.1 to 0.3 gramme ($1\frac{1}{2}$ —5 grains) daily. Pellacani came to the same conclusion, and he found that luminal is still useful when other remedies have failed. He states that doses of 0.2 to 0.8 gramme (3—12 grains) were well borne. In

patients in whom severe epileptic fits still occurred frequently in spite of large doses of bromide (15 to 17 grammes [225 to 255 grains] daily), he stopped the use of bromide and gave luminal. With this treatment he succeeded in reducing the number of fits by one-half in the course of six weeks. If bromide was once more administered the number of fits increased again in an alarming manner. On the other hand, after an interval of a few days luminal displayed its full activity. To almost all the patients he gave doses of 0.2 to 0.3 gramme (3—5 grains) a day, where the fits were very frequent 0.4 to 0.5 gramme (6—7½ grains), and, if necessary, he increased the doses up to 0.6 or 0.7 gramme (9—11 grains).

Frankhauser regards luminal as the remedy of choice when bromine treatment has to be discontinued. It not only prevents the occurrence of the status epilepticus on the sudden withdrawal of bromide, but also markedly diminishes the severity and frequency of the attacks, without producing any cumulative symptoms. The author gave 0.3 gramme (5 grains) for a daily dose. De Moor and Meldola also report equally favourable results.

Pécheux and Lotte studied the sedative action of luminal in four individuals who suffered from frequent attacks of hiccough. Doses of 0.1 to 0.2 gramme (1½—3 grains) of luminal always succeeded in removing this troublesome affliction within a few minutes. Calderon also obtained an immediate success with a dose of 0.3 gramme (5 grains) in an obstinate case which had proved refractory to morphine and atropine.

Magnesium-Perhydrol.

Buttersack states that magnesium-perhydrol is a remedy which is able to influence the glycosuria at least in some diabetics. With five or six daily doses of 0.5 gramme (7½ grains) he succeeded in lowering the excretion of sugar in several of his patients from 4 p. c. to 0.5—0 p. c. Coincident with the decrease in the excretion of sugar there was an amelioration of the general condition, and the patients experienced a gratifying feeling of freshness. On the other hand, glycosuria on a psychic basis, and cases in which the glycosuria was doubtless due to disease of the pancreas, were not influenced to any appreciable extent.

Buttersack also recommends the use of magnesium-perhydrol in the place of sodium bicarbonate for the treatment of gastric conditions, in which the liberation of oxygen, instead of carbonic acid, appears desirable. He has always obtained good results by its use.

Magnesium-perhydrol deserves wider recognition in the treatment of various affections of the digestive tract since it acts as a reliable disinfectant and deodorant by reason of its property of splitting off hydrogen peroxide, or active oxygen. I. Wolpe says that it is especially indicated in hyperacidity, stasis and fermentative dyspepsia. It should also prove useful in meteorism and flatulence, for which it is recommended by P. Cohnheim, who gives 0.5 gramme ($7\frac{1}{2}$ grains) three times daily, after meals, in acid gastritis. Further, the administration of one tablet of magnesium-perhydrol three or four times a day has proved useful in chronic intestinal catarrh, and in colitis and enteritis with sluggishness of the bowels.

Magnesium Sulphate.

Whereas it had hitherto been assumed that the narcotic action of magnesium was due to a peripheral influence on the motor nerves, S. J. Meltzer and J. Auer were able to demonstrate that with magnesium sulphate and ether a summation of the narcotic actions is obtained. They therefore conclude that the magnesium salts display a central (paralysing) action. Whether the results of these experiments on animals can be utilized in practice is still an open question; however, it is quite possible that the combined use of injections of magnesium sulphate and ether inhalations may prove useful in anæsthesia. Although in experiments on rabbits the authors had used insufficient amounts of both drugs, yet they still obtained a full anæsthetic effect. The action of magnesium is also discussed by G. Mansfeld and St. Bosanyi, J. Schütz and E. Starkenstein, but as their papers cannot

Wolpe, *Wratschebnaja Gazeta* 1913, No. 18 and 19.

Cohnheim, *Die Krankheiten des Verdauungskanaals*. Berlin: S. Karger. 1913.

Meltzer-Auer, *Proceedings of the Society for Experimental Biology and Medicine* 1913, Vol. 10, p. 159.

Mansfeld-Bosanyi, *Pflügers Archiv*, Vol. 152, No. 1—3.

Schütz, *Wiener klinische Wochenschrift* 1913, No. 19, p. 745.

Starkenstein, *Wiener klinische Wochenschrift* 1913, No. 30, p. 1235.

well be abstracted reference should be made to the original communications.

Tetanus* still remains a very important indication for injections of magnesium sulphate, and their use is reported upon by Th. Kocher, C. Arnd, A. Dutoit, A. Gottis, H. Letheby Tidy and H. Berger.

Kocher describes three further cases of tetanus** which he treated by injections of magnesium sulphate. In two cases he achieved a cure with six and seven injections respectively. To prevent respiratory paralysis he advises prophylactic tracheotomy, or injections of physostigmine.

Arnd states that up to the present magnesium sulphate has yielded remarkably good results in combating tetanus. However, the dosage still offers difficulties since magnesium sulphate is a drug with an energetic action. The dose proposed by Meltzer of 0.03 gramme per kilogramme body-weight has only an approximate value. If too small a dose is given this can still be rectified within the next few hours, whereas an excessive dose demands special interference before it can be compensated. In two cases he succeeded in effecting this by lumbar puncture and washing out of the meningeal sac and was able to prevent a lethal termination. As regards the concentration of the solution of magnesium sulphate the author believes that it is possible to use still more dilute solutions than are at present employed, but so far no definite data are available concerning intradural injection. Further, it has not yet been established whether another mode of application, e. g., subcutaneous or intravenous injection, may not prove as effective. It should also be taken into account that the toxic symptoms supervening on intravenous injection might be abolished by the intravenous injection of calcium salts. On the other hand, Gottis maintains that the curative value of intralumbar injections of magnesium sulphate has not been conclusively proved, but still he recommends them in tetanus,

* Compare Merck's Reports 1906—1912.

Kocher, *Korrespondenzblatt für Schweizer Ärzte* 1913, p. 97.

Arnd, *Korrespondenzblatt für Schweizer Ärzte* 1913, No. 4.

Dutoit, *Deutsche medizinische Wochenschrift* 1913, No. 12, p. 561.

Gottis, *Thèse de Montpellier* 1912.

Tidy, *British Medical Journal* 1913, I, p. 1104.

Berger, *Berliner klinische Wochenschrift* 1913, No. 44, p. 2047.

** Compare Merck's Report 1912, p. 265.

chorea, sciatica and gastric crises. His experience shows that only mild and transient secondary effects occur. Tidy reports a case of tetanus in a boy, aged eight, who was given an injection of 3 c.c. of a 25 p.c. solution of magnesium sulphate after the withdrawal of 10 c.c. of cerebrospinal fluid. Improvement set in immediately which led to recovery after repeating the injection. Dutoit has published a noteworthy review of the treatment of traumatic tetanus by magnesium sulphate, which should be consulted by those interested in this subject.

Berend used magnesium sulphate in spasmophilia in children, since investigations have shown that this condition is associated not only with disturbances of the calcium and phosphorus metabolism, but also of magnesium metabolism. His trials showed that subcutaneous injections of magnesium sulphate act more promptly than injections of calcium salts. In a great number of the cases treated the convulsions ceased within twenty-four hours.

Rissmann attempted to solve the question whether eclampsia can be cured by intradural injections of magnesium sulphate. In a case described by him in detail he injected 5 c.c. of a 15 p.c. solution, whereupon no further attack occurred. No toxic symptoms were observed. This success induces the author to advocate the further trial of magnesium sulphate.

The use of magnesium sulphate as a subcutaneous purgative is deserving of interest. Carnot was able to show that sodium sulphate is capable of increasing intestinal peristalsis to such a degree that spasms occur, whereas magnesium sulphate inhibits peristalsis and causes an increasing filling of the intestinal loops with transudates. For this reason sodium sulphate would appear indicated in atonic constipation, and magnesium sulphate in spastic constipation. By clinical trials G. Etienne fixed the hypodermic dose at 1 c.c. of a sterilized 25 p.c. solution of magnesium chloride. He reports a few cases in which the subcutaneous injection of 20 c.c. of a

Berend, 85th. Annual Meeting of German Natural Scientists and Physicians, Vienna, 1913. *Münchener medizinische Wochenschrift* 1913, No. 42, p. 2372.

Rissmann, *Zentralblatt für Gynäkologie* 1913, No. 6, p. 196.

Carnot-Etienne, *Le Scalpel*, February 2, 1913, *Wiener klinische Wochenschrift* 1913, No. 13, p. 513.

1 p.c. solution of magnesium sulphate yielded an entirely satisfactory result.

Gaillard also obtained the desired result in the course of seven to eight hours with injections of 0.5 to 1 c.c. of a 25 p.c. solution. Given with due aseptic precautions the injections cause neither pain nor infiltrations and are free from other drawbacks. According to Piñerua, the action sets in after from four to twenty hours, as a rule after ten to twelve hours, otherwise 0.5 c.c. may again be injected on the following day.

The laxative action of magnesium sulphate was investigated pharmacologically by R. Cobet.

According to D. Sieber, magnesium sulphate is of use as an antidote in arsenical poisoning. The author administered to rabbits the lethal dose of arsenic and then made a subcutaneous or intravenous injection of 0.25 to 0.5 gramme of magnesium sulphate per kilogramme body-weight. By this means it was possible to save animals which had been poisoned by the internal or subcutaneous injection of arsenic, but not those poisoned by its intravenous exhibition. The author is unable to explain the action of magnesium sulphate, but he believes that the magnesium sulphate interacts with the arsenic and forms compounds which are with difficulty soluble, or that it delays the passage of the arsenic into the circulation.

Male Fern, Extract of

The action of ethereal extract of male fern on distomatosis in dosmetic animals observed by Raillet, Moussu and Henri has been fully confirmed by the investigations of M. Blanchard. He directs that cattle should be given, according to weight, 10 to 25 grammes ($\frac{1}{3}$ — $\frac{5}{6}$ oz) of extract with 20 grammes ($\frac{2}{3}$ oz) of oil, and sheep 3 to 5 grammes (45—75 grains) with 10 grammes ($\frac{1}{3}$ oz) of oil, and this treatment

Gaillard, Thèse de Paris 1912. — *Revue internationale de médecine* 1913, No. 2, p. 31.

Piñerua, *Revista de medicina y cirujia practicas*, April 28, 1913.
Cobet, *Pflügers Archiv für die gesamte Physiologie*, Vol. 150, No. 6—8.

Sieber, *Archives internationales de pharmacodynamie et de thérapie* 1912, Vol. 22, p. 269.

Blanchard, *Berliner tierärztliche Wochenschrift* 1913, No. 14, p. 256.

should be continued for five days. The drug should be administered in the morning on an empty stomach. The extract is said to have an excellent action and completely destroys the liver flukes, provided it is not given too late. Hence it should be given at the beginning of the infection so long as the liver flukes have attacked only the bile passages and before tissue changes and atrophy of the liver have occurred. If the damage to the tissues has not progressed too far it is still effective in animals which have been cachectic for some time. When the distoma have been expelled by this treatment the changes induced by them heal. On the other hand, if the infection has progressed to such a degree that the liver has lost its capability of function and marked anæmia has set in, nothing can be expected from the use of extract of male fern.

Maretin.

A. Plaut has found maretin a useful remedy for the treatment of articular rheumatism, in which it often yields better results than the salicylates. In view of the fact that several authors, in particular W. Heubner, have stated that it produces bloodlessness, Plaut again undertook a thorough investigation of the drug. In a number of cases he administered for two to four days 0.25 gramme (4 grains) of maretin three or four times daily, usually with good results. The examination of the blood showed that it had no injurious effect. E. Edens, too, in the course of the past six years has used maretin as an antirheumatic with satisfactory results. Especially in cases of rheumatic polyarthrititis which often cannot be benefited even by massive doses of sodium salicylate, maretin per se or combined with salicylates proved an invaluable remedy. On the other hand, the author deprecates its use as a febrifuge in pulmonary tuberculosis, as in this case it would have to be given for a prolonged period, and already after ten to fourteen days' use it produces a yellow coloration, loss of appetite and aggravates the general condition. Moreover, Pitini and Heubner were able to demonstrate by animal

Plaut, *Therapeutische Monatshefte* 1913, No. 7, p. 499.

Heubner, *ibidem*, p. 507, compare also Merck's Report 1911, p. 303.

Edens, *Therapeutische Monatshefte* 1913, No. 7, p. 506.

Pitini, *Archivio di farmacologia e terapia* 1911, p. 109, communicated by Heubner l. c.

experiments that maretin, in distinction to other antipyretics, after prolonged use causes bloodlessness. Therefore Heubner states that maretin should not be given for a prolonged period to the same patient, and only on this condition does he advocate its retention in *materia medica*.

Mastic.

The actual disinfection of the skin, be it of the hands of the operator or of the area of operation, is being more and more abandoned in favour of methods by means of which the bacteria on the skin are so fixed that they cannot penetrate into the wounds. One of these methods is that proposed by von Oettingen of treating the skin with a solution of mastic, which has been frequently dealt with in my Reports*. A. Jaquet, F. Haenel, E. Stierlin and A. Vischer, Treiber and O. Hanasiewicz have recently reported on this method.

Most authors employed mastisol, a solution of mastic of known composition**, and came to the conclusion that sterilisation with solution of mastic is to be reckoned among the best of the methods at present known, and is particularly useful in military surgery; Jaquet gives an exhaustive description of the technique. The hands should be well covered with mastisol and the solvent allowed to evaporate, which takes thirty seconds, whereupon the skin is wiped with sterile cotton wool. The skin is then covered with the cotton wool, which adheres firmly to it, and sterile thread gloves are put on. The skin of the area of operation is treated in the same way and covered with mastic, cotton wool and sterile cloths. In gynaecological operations in which the hands must remain smooth powdered talc in large amounts is used in the place of cotton wool and the hands are lubricated with glycerin, since oil would dissolve the layer of mastic. For details of the procedure the original paper should be consulted.

The use of mastic solution appears to be gaining in fa-

* Compare Merck's Reports 1906—1912.

Jaquet, *Deutsche medizinische Wochenschrift* 1913, No. 42, p. 2044.

Haenel, *Zentralblatt für Chirurgie* 1913, No. 22, p. 863.

Stierlin - Vischer, *Korrespondenzblatt für Schweizer Ärzte* 1913, No. 19.

Treiber, *Psychiatrisch-neurologische Wochenschrift* 1913, p. 504.

Hanasiewicz, *Zentralblatt für Chirurgie* 1913, No. 10, p. 359.

** Merck's Report 1911, p. 303.

your in dermatology. F. Hammer reports upon its use in a case of ulcer of the leg which was situated in tissue of bony hardness and had resisted all attempts at healing, but which gradually became smaller on painting the adjacent parts with mastic. The solution of mastic also proved useful in soft ulcers and buboes, as by its means the extension of the ulcer can be limited by the maceration of the pus. Compared with collodion, the solution of mastic has the advantage that it dries more slowly, does not peel off and does not contract the skin. For this reason it is useful in rhagades at the corners of the mouth, where small strips of gauze can be affixed by its aid. Obstinate fissures of the skin, such as chapped hands and anal fissures, can often only be healed by systematic application of small amounts of dressing. In the treatment of skin diseases Hammer combined the use of solution of mastic with mercuric chloride, tar and chrysarobin; however, on account of its stickiness gauze must be applied and to remove it the skin must be energetically rubbed with benzin. On the other hand, in combination with pyrogallol (10 p.c.) it proved useful in lupus. The use of pyrogallol is less painful in this form than as an ointment and its action is limited to the lupous focus, leaving the surrounding healthy tissue unaffected. The lupous lesions quickly shrink and ulceration is kept within moderate bounds.

Instead of alcohol for disinfecting the site of vaccination Hillenberg tried painting with mastisol, with which he obtained satisfactory results.

In veterinary practice mastisol can be used in the same way as in human practice for fixing dressings. Of course, before applying it to hairy regions the part of the skin must be shaved. Meyer and von Schouppé report on its use in veterinary surgery.

Melubrin.

Further contributions regarding the action of melubrin* in articular rheumatism have been published by K. Loening,

Hammer, *Dermatologische Wochenschrift* 1913, No. 21, p. 518.

Hillenberg, *Zeitschrift für Medizinalbeamte* 1913, No. 17.

Meyer, *Zeitschrift für Veterinärkunde* 1913, No. 11, p. 499.

Schouppé, *Tierärztliches Zentralblatt* 1913, No. 2.

* Compare Merck's Report 1912.

Loening, *Therapeutische Monatshefte* 1913, No. 2, p. 123.

E. Keuper, M. Schmid, Klare, K. Riedel, B. Hahn and Schultze.

In two cases of subacute articular rheumatism Schmid gave up to six doses daily of 0.5 gramme ($7\frac{1}{2}$ grains) of melubrin, in addition to brine baths and electric light baths, with the result that the acute inflammatory manifestations subsided. In the same way the acute attacks of pains in simple articular rheumatism usually disappeared promptly. The drug also proved useful in chronic muscular rheumatism. Keuper also prescribed it for acute and chronic muscular rheumatism. Although in these cases it is difficult to gauge the effect of drugs, yet the author never met with a failure and always observed a prompt action without any drawbacks. The other above cited authors also express a favourable opinion of the value of melubrin.

In the place of oral administration Hahn advocates the intravenous injection of melubrin in patients with a sensitive gastro-intestinal tract, and also in those cases which are difficult to influence by internal medication. For this purpose a 50 p.c. sterile solution is used of which 2.5 to 3 grammes are injected three times daily. Riedel confirms the good action of injections of melubrin, but in view of their frequent repetition he considers this method too troublesome and therefore suggests the use of intramuscular injections of the drug. It is possible to inject into the glutei 2 to 3 grammes (30—45 grains) of melubrin three times a day without inconvenience to the patient; the author has even given 4 to 5 grammes (60 to 75 grains) of melubrin twice a day without any secondary effects. The analgesic action frequently manifests itself within fifteen to thirty minutes after the injection. The articular swellings also soon subside. Riedel states that the antipyretic effect of melubrin was always satisfactory. The fever gradually declined in a curve within six to eight hours by 1.5° to 2° C., to then rise by 0.7° to 1° C. The 50 p.c. solution can also be used for subcutaneous injection, but care must be taken to prescribe it as follows, to prevent an overdose:

Keuper, Deutsche medizinische Wochenschrift 1913, No. 18, p. 835.

Schmid, *ibid.* 1913, No. 23, p. 1095.

Klare, *ibid.* 1913, No. 33, p. 1616.

Riedel, Münchener medizinische Wochenschrift 1913, No. 44, p. 2454.

Hahn, *ibid.* 1913, No. 40, p. 2232.

Schultze, Medizinische Klinik 1913, No. 11, p. 416.

Rp. Melubrin. pulv. 7.5 grammes

Aq. dest. ad 15 c. c.

M. Sig.: 1 syringeful three times daily. For subcutaneous (intramuscular) injection.

The yellow colour which appears while sterilizing the solution is, according to Hahn and Riedel, without influence on the action of melubrin.

Melubrin is worthy of recognition in the treatment of morbus maculosus Werlhofii, chorea minor and pleuritic exudates; Keuper states that it proved very useful in some cases.

Melubrin is a good antipyretic in tuberculosis. O. Hesse states that it permits a great latitude in dosage and can be given for weeks without having to fear the occurrence of secondary effects, with the exception of sweating. Collapse temperature is possible if too large a dose is given. Amounts of 0.25 to 1 gramme (4—15 grains), once to thrice daily, are given to adults; the usual dose is 0.5 gramme ($7\frac{1}{2}$ grains), but it is necessary to individualize. Hesse states that the above mentioned doses of melubrin fairly often proved ineffective.

For the pains which occur during treatment with radium emanations E. Wollenberg prescribed two tablets of melubrin three times a day, for two or three days. By giving melubrin the treatment could be continued without interruption, since the drug succeeded in alleviating the pains.

Schuster tried melubrin in whooping-cough. He gave it to children of six months to four years of age in corresponding doses for about three weeks. It was well borne and was of value in reducing the number and severity of the attacks, but did not effect a complete recovery. The author also used it with good results in other diseases, such as articular rheumatism, tuberculosis, and arthritis not due to rheumatism. He reports that in the majority of cases it causes no derangement of the organic functions, and even in the presence of slight gastric disturbances and albuminuria no undesirable sequelæ were observed. Mild cases of acute gastric and intestinal catarrh were usually beneficially influenced. However, in some cases vomiting, nausea and diarrhœa made it necessary to

Hesse, Therapie der Gegenwart 1913, No. 2, p. 68.

Wollenberg, Medizinische Klinik 1913, No. 2, p. 63.

Schuster, Deutsche medizinische Wochenschrift 1913, No. 7, p. 310.

stop the use of the drug. Moreover, the occurrence of profuse sweating in the tertiary stage of pulmonary tuberculosis proved a drawback.

Menthol.

Subjective noises in the ear of non-organic origin, which usually occur on a neurasthenic basis and after repeated attacks of middle-ear catarrh, are treated by M. Peltzer by valyl and menthol oil. By means of a pledget of cotton wool he introduces a solution of menthol in olive oil (5:100) deep into the external auditory canal, and gives two or three valyl perles two or three times daily, after meals. It is advisable to alternate the use of valyl, menthol oil and Roman baths, measures which ensure a long period of rest, and by these means the patient is accustomed to pay less heed to the noises and convince himself of their harmlessness.

As I have already reported*, the treatment of pulmonary tuberculosis with inunctions according to Stepp's method has been found very effective. The author has continued his experiments, but now he uses the following mixture in the place of the menthol-eucerin ointment:

Rp. Menthol.	10 grammes ($\frac{1}{3}$ oz)
Thymol.	2 „ (30 grains)
Sap. moll.	30 „ (1 oz)
M. Ft. ung.	

Menthol and thymol yield a liquid which can be worked up into a pliant ointment with the soft soap. This amount is sufficient for five days' treatment. It is applied as follows: On the first day one teaspoonful is rubbed into one half of the back, and on the second day into the other half, on the third day into the chest, on the fourth and fifth days it is applied to the right and left thigh respectively, and the rubbing is continued for eight minutes. It is allowed to remain on the skin for twenty-four hours, whereupon it is washed off with lukewarm water. To prevent roughness of the skin it is then dried and olive oil is applied. As a rule, already after eight to ten days' treatment the effect is said to become manifest in the second stage of pulmonary tuberculosis. The dullness

Peltzer, Fortschritte der Medizin 1913, No. 35, p. 970.

* Compare Merck's Report 1910, p. 248.

Stepp, Fortschritte der Medizin 1913, No. 31, p. 841.

diminishes, and the note to percussion becomes tympanitic, roughness in the breath sounds, or the bronchial respiration, as well as the râles diminish, and the appearance of the sputum improves. The treatment is continued for two or three months, often longer. Considerable improvement can also be effected in the third stage of the disease. Especially in children and young persons this treatment is said to yield ideal results; the tuberculous infiltration disappears entirely and does not return. If in certain cases the fever present from the beginning does not subside under this treatment, this is evidence of acute tuberculous processes or of caseous foci.

Tuberculosis of the bones is also beneficially influenced by this treatment with inunctions; on the other hand, it fails in acute tuberculosis, acute tuberculous pneumonia and in pulmonary tuberculosis following on diabetes.

E. Pasch recommends the use of menthol in another form and combination for the treatment of pulmonary tuberculosis. He causes it to be inhaled in combination with oil of turpentine, eucalyptus oil and oil of pine, so-called "terpino-menth". The author obtained satisfactory results with this combination in a number of cases of acute coryza, ozæna and sinusitis, retronasal catarrh, acute and chronic pharyngitis and laryngitis, pharyngo-laryngitis and tracheitis, some of which were complicated with tuberculosis.

Dioradin*, another preparation containing menthol and which has already been discussed in these Reports, was tried in tuberculosis by Atkinson Stoney. He states that it is not suitable in all cases of tuberculosis; in some instances, however, the preparation displays a quicker and more reliable action than other methods of treatment.

Menthospirin.

This is the name applied by J. Loewenheim to the acetyl-salicylic acid ester of menthol, a light yellow, thick fluid which is hydrolysed by water. It is insoluble in water, soluble in alcohol, ether and fatty oils. Its chemical composition is: $\text{CH}_3\text{COO} \cdot \text{C}_6\text{H}_4 \cdot \text{COO} \cdot \text{C}_{10}\text{H}_{19}$. It is issued in

Pasch, Allgemeine medizinische Zentralzeitung 1913, No. 9, p. 101.

* Merck's Report 1911 and 1912.

Stoney, British Medical Journal 1913, I., p. 215.

Loewenheim, Medizinische Klinik 1913, No. 19, p. 751.

gelatin perles containing 0.25 grammes (4 grains) of the preparation.

The pharmacological investigation of the preparation undertaken by Boruttau showed that in the organism it is slowly split up into its components, whereupon the anæsthetising and analgesic action of menthol on the mucous membranes of the respiratory passages becomes manifest, as well as its stimulating effect on the heart's action, in addition to the sedative and antifebrile action of acetyl-salicylic acid.

Loewenheim prescribed menthospirin in acute and subacute catarrhs ensuing on infection and "colds", and he found that the action of the preparation came up to his expectations. In every case the author observed a rapid abatement of the fever and subsidence of the inflammatory manifestations. The feeling of pressure and the pain in the forehead, as well as the pains in the ears, were quickly relieved. As a rule, the author gave to adults two or three capsules, two or three times daily.

In laryngeal tuberculosis menthospirin apparently is more effective than menthol. Loewenheim tried injections of the preparation in oily solution, but was unable to form a conclusive opinion of the value of this method of treatment.

The internal use of menthospirin is capable of alleviating and shortening the discomfort associated with hay fever. M. Wolfheim reports some cases in which the preparation, given in daily doses of 4 grammes (60 grains), proved useful.

Mercury Oxycyanide.

In the treatment of severe post-operative inflammations of the eye Hirsch has used with advantage a solution of mercury oxycyanide* containing acoine. He employed it in cases of painful inflammation of the ciliary body involving the first trigeminus, in which an injection of a solution containing 1 p.c. of mercury oxycyanide and 0.4 p.c. of acoine, made into the back, removed the pains almost immediately. The photophobia and inflammatory manifestations also subsided

Boruttau, communicated by Loewenheim.

Wolfheim, *Therapie der Gegenwart* 1913, No. 10, p. 478.

Hirsch, *Wochenschrift für Therapie und Hygiene des Auges* 1912, No. 22.

* Merck's Report 1907, p. 128.

after the injection. According to Hirsch, a few injections suffice to save a eye threatened with panophthalmia.

In a further communication Hirsch points out that injections of mercury oxycyanide are also capable of displaying a similar action in other cases of inflammation and pain referable to peripheral nerves, for instance in tabetic crises which are solely due to peripheral neuritis or perineuritis. Since in tabes the visual apparatus is frequently involved and such patients are seen by the oculist in all stages of the disease, the author undertook experiments which showed that in girdle pains, intercostal neuralgia and other neuralgias "Hirsch's injection" is capable of abolishing the pains of tabetic origin. Of course, it is incapable of influencing completed anatomical post-syphilitic degenerations and old-standing paralysis of a muscle of the eye.

In a case of pseudo-tabes, due to alcoholic neuritis, Hirsch also obtained a speedy recovery by means of his injection. However, it failed in an elderly non-syphilitic patient with multiple phenomena of paralysis referable to the medulla oblongata, and even caused an aggravation of the general condition.

In several cases of supra-orbital neuralgias of indefinite etiology the injection always succeeded in immediately abolishing the pain. In some cases further attacks remained absent only on repeating the injection several times.

H. Kühl has published an interesting work on the antiseptic value of mercury oxycyanide and of mercury oxycyanide according to Holdermann*, which cannot be briefly abstracted, and for details the original should be consulted. It may be mentioned that the results of the author's investigations show that both preparations have an equally effective disinfectant action.

Mercury Salicylate.

Mercury salicylate is undoubtedly one of the most extensively used preparations of mercury among those employed for the intramuscular treatment of syphilis. Like all insoluble

Hirsch, *Münchener medizinische Wochenschrift* 1913, No. 19, p. 1036.
Kühl, *Archiv der Pharmazie* 1913, No. 5. — *Süddeutsche Apotheker-Zeitung* 1913, No. 84, p. 688.

* Compare Merck's Index 1910, p. 144.

compounds of mercury its injection frequently gives rise to pain, and for this reason Wollheim attempted to render the suspension of mercury salicylate used for injection painless by the use of a suitable vehicle and by the addition of certain compounds. He tried a series of suspensions to which he added quinine and urea hydrochloride for the purpose of producing anæsthesia by means of these additions, as had been successfully accomplished by Walson for injections of mercuric chloride. Both compounds have the advantage that they are non-toxic, and that they do not cause habituation. Wollheim states that the following mixture yielded the best results:

Rp. Quinin. sulph.	2 grammes
Ureæ hydrochlor.	2 „
Adip. lan. anhydr.	20 „
Aq. dest.	2 „
Hydrargyr. salicyl.	10 „
Paraffin. liq.	ad 100 „

The quinine sulphate and the urea hydrochloride are dissolved in the stated amount of water, and the solution is mixed with the wool fat, whereupon the mercury salicylate is rubbed down with the mixture, and then the liquid paraffin is added. After using this mixture in a large number of cases the author came to the conclusion that the percentage of cases which reacted by pains showed a considerable decrease. Whereas the ordinary suspension was borne without much pain in only 33 p.c. of the cases, the use of the above combination proved painless in 83 p.c. of the cases treated.

Mergal.

According to R. Peters, mercury is still the best remedy for combating syphilis, as he was able to establish in a very large number of cases. In the author's opinion occasional failures are due to the fact that it is not given in sufficient amounts and for too short a time, and is usually stopped when the demonstrable manifestations have disappeared, and further to the fact that it causes toxic secondary effects which make it necessary to interrupt treatment. However, it is possible to completely destroy the causal germs of the disease

Wollheim, Merck's Archives 1912, p. 251.

Peters, Wiener klinische Rundschau 1913, No. 47, p. 826.

only when mercury is continuously administered. Since for the above stated reasons treatment by inunctions and injections cannot be carried out without interruption, the author advocates the use of a method which permits a continuation of mercurial treatment by the use of milder and better tolerated drugs, whereby efficient treatment can be interposed between the series of inunctions and injections. After trials extending over several years the author found mergal* to be best suited for this purpose. It is as a rule well borne, and only in a very small percentage of cases its use has to be stopped owing to extreme susceptibility of the patients.

In primary manifestations mergal treatment should, under all circumstances, be preceded by an energetic treatment by inunctions or injections, since in these cases the use of mergal alone rarely yields the desired result. In one case out of twenty the author succeeded in transforming a positive Wassermann reaction into a permanent negative reaction, and in preventing the occurrence of secondary manifestations.

Mergal is especially indicated in secondary manifestations, since in these cases to obtain a cure the negative Wassermann reaction must be maintained for months and the organism must be kept constantly under the action of mercury.

In tertiary syphilis with external or skin manifestations the author considers mergal an indispensable remedy with a prompt and reliable action. On the other hand, he failed to observe any success in affections of the nervous system. However, a successful result may be obtained by the simultaneous use of large doses of iodine.

Merjodin.

R. Polland undertook experiments for the purpose of comparing the elimination of various mercurial preparations intended for internal use, and he found that with merjodin** alone the amount of mercury appearing in the urine stood in a correct ratio to the amount of merjodin ingested, and was almost as large as following a mild course of treatment with inunctions. From this the author concludes that merjodin

* Compare Merck's Reports 1906—1911.

Polland, Münchener medizinische Wochenschrift 1913, No. 11, p. 590.

Compare also Österreichische Ärzte-Zeitung 1910, No. 9, p. 194.

** Compare Merck's Report 1911, p. 313.

is well absorbed, without producing any local symptoms of irritation worthy of mention. The preparation is suited for carrying out a course of internal mercurial treatment since large amounts of mercury are introduced into the circulation. The author's results are in keeping with his previous findings which he published some years ago. He stated at the time that merjodin is a useful preparation which yields satisfactory symptomatic results when given in daily doses of five or six tablets, using altogether 150 to 200 tablets. The results correspond with those obtained by a mild course of inunctions. The author states that the iodine content of merjodin (mercury diiodo-para-phenolsulphonate) has a certain influence in increasing the action of mercury. It neither hastens nor retards the elimination of mercury, but apparently reduces the risk of mercurial intoxication.

In experiments with merjodin and mercury-glidine undertaken on women A. Horn came to the conclusion that both preparations, even when used in conjunction with inunctions, did not comply with the demands to be made of them. Their use neither shortened the duration of treatment nor did it increase the number of negative Wassermann reactions. Both preparations are, in his opinion, as little suited for the treatment of fresh syphilis as is mergal. The secondary effects are mild and transient, in keeping with the content of mercury.

Mesothorium.

As is apparent from the publications which have appeared during the past year treatment with the rays given off by mesothorium* marks a further important advance in the cure of cancer. E. Bumm points out that by appropriate filtration and the use of suitable hard tubes it is now possible to apply far larger amounts of active rays in larger cavities without injury to healthy tissue, and thereby to produce appreciably greater therapeutic effects than was hitherto possible. Further, the production of mesothorium on a commercial scale now makes it possible to expose the

Horn, Dissertation Würzburg 1913. — Deutsche medizinische Wochenschrift 1913, No. 47, p. 2320.

* Compare Merck's Report 1912, p. 280.

Bumm, Berliner klinische Wochenschrift 1913, No. 22, p. 1001.

deeper parts of cavities, where Röntgenization is difficult, to the action of larger amounts of radio-active substances. Basing on the records of his cases, Bumm states that the treatment and cure, or the transformation of inoperable cases of carcinoma of the uterus into operable cases, has a great future. From these it is apparent that in some cases of carcinoma of the genitals irradiation by mesothorium yields results which exhibit the clinical picture of a cure. Whether a definite cure has been achieved cannot be established at present. Nevertheless, there is no doubt that wherever X rays, radium or mesothorium rays impinge on the tissue with a certain intensity the carcinomatous neoplasms are destroyed. Bumm states that this is especially the case with hard carcinomata, cancrroids and squamous-celled epithelioma with abundant stroma, but soft cancers and cancers of the glands and mucous membranes form no exception. "Wherever it is possible to apply a sufficiently large amount of rays the cancer cells are destroyed with formation of vacuoles and disintegration of the nuclei." This result is obtainable within a relatively short time. Thus, in one case after nine days the cancerous foci were already severely damaged to a depth of 1 cm. and were in part breaking down; in another case no intact cancer nests were present after twenty-four hours and 13,000 milligramme-hours of mesothorium. In practice the author considers operative removal of the new growth to be still the surest course in younger individuals with rapidly growing carcinomata of the uterus, since with this procedure the lymphatic glands are also removed, which are difficult to influence by irradiation. This should be followed by irradiation of the scar and of the neighbourhood of the cancerous focus, in which the majority of recurrences occur. At the conclusion of his work Bumm says: "Already now we may undertake with confidence irradiation of carcinomata of the vagina, of the external genitals and of the urethra. The same applies to slowly developing cancerous tumours at the collum uteri in elderly women. All these more or less superficially situated new growths may easily be rendered accessible to irradiations, if necessary by the help of supplementary incisions, and the result is a better clinical cure than following an operation, inasmuch as the function of the part remains unimpaired. In inoperable carcinoma of the genitals irradiation yields more satisfactory results than any

other at present known method of treatment, and even in recurrences after operation it is preferable to another operation. A second operation is extremely likely to favour excessive proliferation, whereas irradiation, as a rule, is followed by an unexpectedly rapid shrinkage and subsidence of the new growths, leading to a clinical cure."

Basing on their experience, Krönig and Gauss advocate the following treatment of carcinoma: When the carcinoma is still operable and is amenable to control by the senses of touch and smell, an attempt should be made to effect a cure by irradiation. If no success ensues, it is still early enough to perform an operation. If the carcinoma is operable, but not amenable to the above mentioned control; then a radical operation may be performed if the assumptive index for primary mortality of operation and absolute permanency of result holds out a promise of success, otherwise treatment with irradiations is indicated. If the carcinoma is inoperable intensive irradiation must be applied under all circumstances and its action should be assisted by combining it with other related methods of treatment. Every case of operative treatment should be followed by a prophylactic, systematic course of irradiations, which should be repeated at certain intervals.

A. Pinkuss also advocates irradiation after a radical operation in order to prevent as far as possible recurrences. Moreover, he emphasises the value of combining treatment with irradiations with other procedures holding out a promise of influencing the cancerous affection within the body, in particular with intravenous injections of atoxyl and thorium X, as well as the internal use of thorium X and pancreatin. His experience extends to 8 cases of carcinomata of the uterus and vagina, 11 cases of mammary carcinoma, 1 recurrence of cancer of the rectum and 1 recurrence of cancer of the ovaries, all of which had not yet reached the advanced stage of cancerous cachexia. S. Meidner also records a case of carcinoma of the portio which was profoundly influenced by mesothorium treatment. In addition, mention may be made of the following publications dealing with the treatment of cancer by mesothorium:

Krönig-Gauss, Deutsche medizinische Wochenschrift 1913, No. 26, p. 1234.

Meidner, Therapie der Gegenwart 1913, No. 4, p. 149.

- Caan, Münchener medizinische Wochenschrift 1913, No. 1, p. 9.
Pinkuss, Deutsche medizinische Wochenschrift 1913, No. 21, p. 1007.
Saalfeld, Berliner klinische Wochenschrift 1913, No. 4, p. 166.
Hoffmann, Therapie der Gegenwart 1913, No. 6, p. 269.
Meidner, Therapie der Gegenwart 1913, No. 6, p. 274 and No. 10, p. 447.
Sigwart and P. Haendly, Medizinische Klinik 1913, No. 33, p. 1322.
Pinkuss, Deutsche medizinische Wochenschrift 1913, No. 36, p. 1720.
Meidner, Therapie der Gegenwart 1913, No. 9, p. 406.
Schindler, Wiener klinische Wochenschrift 1913, No. 36, p. 1413.
Döderlein, Monatsschrift für Geburtshilfe und Gynäkologie 1913, No. 5. — Berliner klinische Wochenschrift 1913, No. 22, p. 1031.
Haendly, Berliner klinische Wochenschrift 1913, No. 22, p. 1033.
Kroemer, Münchener medizinische Wochenschrift 1913, No. 26, p. 1455.
Bumm, Krönig-Gauss, Döderlein, Haendly, Krömer, v. Franqué and others, Zentralblatt für Gynäkologie 1913, No. 24, p. 889—900.
Adler, Wiener klinische Wochenschrift 1913, No. 26, p. 1093.
Sticker, Strahlentherapie 1913, Vol. 3, p. 1.
Bumm and H. Voigts, Münchener medizinische Wochenschrift 1913, No. 31, p. 1697.
v. Seuffert, Strahlentherapie 1913, Vol. 2, p. 729.
Wanner-Teutschländer, Monatsschrift für Geburtshilfe und Gynäkologie 1913, Vol. 38, p. 296.
Blumberg, Berliner klinische Wochenschrift 1913, No. 49, p. 2299.
Allmann, Deutsche medizinische Wochenschrift 1913, No. 49, p. 2402.
Lobenhoffer, Beiträge zur klinischen Chirurgie 1913, Vol. 87, No. 2.

Mesothorium treatment is also useful in hæmorrhagic metropathies and in myomata. According to A. Pinkuss, it holds out a promise, in the same way as deep Röntgenization, of checking the bleeding and in many cases it obviates the necessity for extensive surgical operations. Under this treatment it is possible to bring about amenorrhœa or oligomenorrhœa through atrophy of the ovaries, whereby the symptoms due to abolition of the latter are milder than following operative castration. It is especially indicated during the time approaching the menopause. Its application is also easier and more convenient than X ray treatment, which is apparently less effective. Voigts expresses an equally favourable opinion of mesothorium treatment and its value in bleeding at the climacteric, in metritis, menorrhagia, and hæmorrhages due to affections of the appendages and to myomata. Gauss and Krinski are also well satisfied with the action of mesothorium treatment in myomata.

- Pinkuss, Deutsche medizinische Wochenschrift 1913, No. 22, p. 1041.
Voigts, Münchener medizinische Wochenschrift 1913, No. 22, p. 1188.
Gauss-Krinski, *ibidem* 1913, No. 25, p. 1404.

In applying mesothorium it must be borne in mind that, like radium, the preparation is injurious to germ cells, and, according to M. Simmonds, large doses may even cause their complete destruction with consequent loss of procreative capacity. It therefore follows that in applying mesothorium the patient must be protected against its injurious effects; further, however carefully mesothorium may be packed it should never be carried about in the pocket.

Various skin diseases afford a further indication for mesothorium. In specially selected cases and with careful technique mesothorium treatment promises to prove very useful in dermatology, for instance in lupus vulgaris and erythematosis, psoriasis, chronic eczema, neuralgias and tuberculosis of the bones. However, P. Wichmann found that in psoriasis and eczema greater care must be exercised than with radium treatment, since mesothorium has a more powerful effect and an irritant superficial action. The technique and results are discussed by E. Kunitzky, O.E. Nägeli and M. Jessner. Mesothorium is applied in a tube, in the same way as radium, and according to the depth of the skin affection to be treated the application lasts for from twenty minutes to two hours. With this treatment Kunitzky succeeded in effecting a cure, or a marked improvement, in epithelioma, naevi, warts, lupus, etc. Nägeli irradiated lupus vulgaris for 30 to 45 minutes and in some of his cases achieved satisfactory results, while others did not benefit. On the other hand, cases of lupus erythematosis were almost without exception very favourably influenced. Further, the results were highly satisfactory in epitheliomata, non-parasitic sycosis, psoriasis, lupus pernio and granuloma annulare, satisfactory in raised angiomas, naevi angiomas, naevi aranei and verrucæ planæ juveniles; in naevi pigmentosi and pilosi the cosmetic result was disappointing. The treatment of hyperkeratotic processes, such as clavi, verrucæ duræ and planæ, and tuberculosis verrucosa cutis, presented greater difficulties.

Simmonds, Deutsche medizinische Wochenschrift 1913, No. 47, p. 2292.

Wichmann, Strahlentherapie 1912, Vol. 1, p. 483. Comp. Lautsch,

Deutsche medizinische Wochenschrift 1913, No. 50, p. 2487.

Kunitzky, Archiv für Dermatologie 1913, Vol. 116, No. 2.

Nägeli-Jessner, Therapeutische Monatshefte 1913, No. 11, p. 765.

In sciatica, tabes and chronic affections of the joints F. Freund and A. Kriser undertook experiments in collaboration with Falta* in which they used the mesothorium mud which occurs as a side product in the extraction of thorium from monazite. It forms a grey, unctuous mass, without smell, with a pronounced metallic lustre, and contains mesothorium and radium. So as not to have to throw away the mud each time after use, the authors employed it in a dry state, packed in bags of kid, whereby the greatest part of the α rays were cut off. As a rule about 100 to 200 grammes, enclosed in a bag the size of a post card and wrapped round with a layer of gauze, were fixed to the affected part by means of a calico bandage. This was applied daily for two hours, in several cases for four to six hours. No injury to the skin was observed. In sciatica the effect of this treatment was very satisfactory, and was especially marked in relieving the pain. In affections of the joints a marked success was obtained only in one case of rheumatismus partialis, whereas the other cases derived only slight, transient benefit, or none at all. In tabes this treatment was tried without success. On the other hand, trials with it in chronic tendovaginitis and pruritus ani seem indicated.

Görges tried a similar method in gout, gouty neuralgias, non-acute articular rheumatism, rheumatic neuralgias and arthritis deformans. He made use of pads made of English lint which were filled with asbestos impregnated with mesothorium and moistened with solution of sodium chloride, and which were applied to the painful parts. The size of the pads was 20×40 cm., and they contained 0.4 to 1.2 milligramme of mesothorium; the application lasted for from one to twelve hours. The results were in part satisfactory, some indeed surprising, but in some cases this treatment failed.

N. J. Cuperus reports on the use of mesothorium in ophthalmology. The use of mesothorium in amounts of 4 milligrammes for irradiation lasting from five to fifteen minutes yielded good results in diffuse scrofulous keratitis, tuberculous

Freund-Kriser-Falta, *Therapeutische Monatshefte* 1913, No. 4, p. 282.

* Compare Görges, *Münchener medizinische Wochenschrift* 1913, No. 26, p. 1467.

Görges, *Berliner klinische Wochenschrift* 1913, No. 29, p. 1345.

Cuperus, *Nederlandsch Tijdschrift voor Geneeskunde* 1913, No. 8.

iritis, ulcer of the cornea, keratitis pannosa, chronic blepharitis, trachoma, recent corneal leukoma, etc.

Hugel's statements show that mesothorium deserves consideration in otology in the treatment of difficulty of hearing and in tinnitus.

Methylene Blue, Medicinal*.

R. Fleckseder reports a case of infectious jaundice which could not be influenced by the customary classical treatment. However, the manifestations soon yielded under treatment by three daily doses of 0.1 gramme ($1\frac{1}{2}$ grains) of methylene blue. The author states that a similar success is obtainable by the use of the preparation in obstinate cases of syphilitic and catarrhal jaundice. In these cases 0.1 to 0.2 gramme ($1\frac{1}{2}$ —3 grains) of methylene blue is given three or four times daily, in gelatin capsules.

β -Naphthol.

I. van der Hoeve states that in dogs and rabbits the percutaneous, subcutaneous or internal administration of large doses of naphthol causes the formation of small white circumscribed foci in the retina, which in the course of time become pigmented. If the administration of naphthol is continued the foci become larger and tend to run together. In addition, there is dilatation of the vessels and hyperæmia of the pupil. Lenticular changes were not always seen, and sometimes there was only irregular refraction, frequently partial cataract ensued. Further, turbidity of the aqueous humour and of the vitreous is also observed, but the latter clears up later, even if the intoxication is continued. No inflammation could be demonstrated in the retina, but only signs of degeneration which also occurred in internal organs such as the kidneys, liver, heart and spleen. These findings in animal experiments were to some extent also observed in persons suffering from scabies in whom 50 grammes ($1\frac{3}{4}$ oz) of a 7.5 p.c. naphthol ointment had been rubbed into the whole surface of the body. After two days hyperæmia of the fundus

Hugel, Münchener medizinische Wochenschrift 1913, No. 38, p. 2110.

* See also the article on Silver Methylene Blue in this Report. Fleckseder, Münchener medizinische Wochenschrift 1913, No. 25, p. 1213. — Revue de thérapeutique 1913, No. 14, p. 488.

Hoeve, Archiv für Ophthalmologie 1913, Vol. 85, p. 305.

supervened, and in one out of twenty cases punctiform turbidity of the lens occurred, and in two cases turbidity of the vitreous with mostly pigmented foci on the retina, which in two cases caused a marked loss of visual power.

F. M. Litterscheid gives the following test for the presence of technical invert sugar in honey. 10 to 20 grammes of the honey to be tested are rubbed down twice with 10 c. c. of ether, in which two crystals of β -naphthol have been dissolved. The ether is filtered into a flat porcelain capsule and is allowed to evaporate spontaneously, in a place protected from light. 4 to 5 c. c. of sulphuric acid (88—90 p. c.) are layered on to the residue and the whole is placed on one side. In the presence of technical invert sugar the contents of the capsule develop a claret to bluish-violet colour in the course of half an hour; if the honey is free from technical invert sugar only a dirty yellowish colour appears, which occasionally changes to red, and after half an hour to a dirty yellowish-green.

W. D. Konopliankin records his experience of the naphthol-camphor* treatment of tuberculous lymphadenitis. After aspiration of the pus he injected the preparation in a 3 p. c. emulsion and was extremely satisfied with the results.

Narcophin.

The use of narcophin** in obstetrics appears to command special interest, as is apparent from the communications by H. Rosenthal, R. Th. Jaschke and H. Drews. Rosenthal states that narcophin has the advantage over morphine of displaying a more continuous action, and is better tolerated. According to his report it proved especially useful in parturition. At the beginning of labour, when the pains commence to become painful, he injected 0.03 gramme ($\frac{1}{2}$ grain) of narcophin subcutaneously. This dose is followed by a welcome feeling of lassitude and during the intervals between labour

Litterscheid, Chemiker-Zeitung 1913, Vol. 32, p. 321.

Konopliankin, Wojenno Medizinskij Journal 1913, Vol. 238, p. 11.

* Compare Merck's Report 1908, p. 256.

** Compare Merck's Report 1912, p. 296.

Rosenthal, Münchener medizinische Wochenschrift 1913, No. 34, p. 1917.

Jaschke, Münchener medizinische Wochenschrift 1913, No. 2, p. 72.

Drews, Zentralblatt für Gynäkologie 1913, No. 20, p. 717.

pains the patients lie in a slightly dazed state and do not experience any particularly severe pain during the expulsion period. Undesirable side effects such as prolonged labour or asphyxia of the child were not observed. Jaschke states that he did not observe any secondary hæmorrhage or disturbances referable to the intestines or bladder; the secretion of milk was not influenced. He also made the observation that with narcophin it is possible to reduce the labour pains to such an extent that they are bearable even for sensitive women. Drews confirms the value of narcophin in painful labour pains, but he believes that it often exposes the child to grave risks, since in three cases out of twenty-five the children were born asphyxiated. Therefore, he regards it as imperative to control most carefully the child's heart sounds. Further, before making the injection the stage of labour must be carefully considered, for the author found that when narcophin is given in the period of dilatation it displays an action similar to that of morphine, and the functions of labour pains cease entirely. On the other hand, given during the period of expulsion it markedly relieved the pains, and the activity of labour pains was not unfavourably influenced.

In cases in which it is desirable to hasten delivery as much as possible, as in the presence of fever, Drews recommends the use of a combination of narcophin and pituitrin. He directs that 1 c.c. of a 3 p.c. solution of narcophin should first be injected, followed a quarter to half an hour later by a subcutaneous injection of 1 c.c. of pituitrin. The action of narcophin manifests itself after about thirty minutes, and if necessary another injection of 0.5 c.c. may be given. Drews states that narcophin is also of use in abortion. In threatened abortion 25 drops are given three times daily*.

According to Rosenthal, narcophin is likewise very useful as a sedative before operations, and also as an analgesic and soporific. In cases where a prompt analgesic effect is desired the use of morphine is preferable, e. g., in biliary and renal colic and in tabetic crises. On the other hand, in conditions of excitement and in the cough of phthisis, in which a lengthy action is indicated, narcophin is to be preferred; this is particularly the case when morphine causes attacks

* The author does not state the strength of the solution, but doubtless the 3 p.c. solution is meant.

of giddiness or vomiting. For this reason Wockenfuss advocates its use, inter alia, in neuralgias (sciatica). G. Eisner also expresses a favourable opinion of narcophin. He prescribed it in tablets of 0.015 gramme ($\frac{1}{4}$ grain), and injections of 0.015 and 0.03 gramme ($\frac{1}{4}$ and $\frac{1}{2}$ grain), or doses of 15 to 25 drops of a 2 p. c. solution.

Neo-Bornyval.

This preparation was briefly discussed in my last year's Report, when I pointed out that it has the advantage over bornyval of being better tolerated. According to Engelen, the sedative action of both preparations is the same, as the author was able to observe in the treatment of hysteria, neurasthenia, nervous restlessness due to over-exertion, etc. In the course of these trials Engelen found that neo-bornyval displays a prompt effect also in cardiac neurosis. His patients stated that the use of this remedy quickly led to an improvement of the subjective signs, e. g., the attacks of palpitation of the heart, the nervous anxiety, etc. The author was able to demonstrate the action of neo-bornyval on nervous disturbances of circulation by experiments and by tracings showing the changes in volume of the pulse.

Rigler also prescribed neo-bornyval in cardiac neuroses, and in neurasthenia, hysteria, formes frustes of Graves's disease, and traumatic neuroses. In all his cases he gained the impression that neo-bornyval displays a marked sedative effect on the nervous system and that it is a better adjuvant to physical and dietetic methods of treatment than tincture of valerian. If it is desired to avoid the eructation which occasionally occurs after taking the preparation it should be taken with the meals. To obtain a permanent success it is essential to administer neo-bornyval for a prolonged period, beginning with small doses and gradually increasing the doses. The use of the drug should not be suddenly stopped, but should be continued by giving two or three perles of neo-bornyval daily for some time. It is not necessary to give more than eight perles daily to obtain a satisfactory end-result.

Wockenfuss, Münchener medizinische Wochenschrift 1913, Nr. 38, p. 2150.
Eisner, Therapeutische Monatshefte 1913, No. 5, p. 353.
Engelen, Deutsche medizinische Wochenschrift 1913, No. 34, p. 1642.
Rigler, Münchener medizinische Wochenschrift 1913, No. 5, p. 249.

Neosalvarsan.

To offer even a condensed review of the entire literature on neosalvarsan within the limits of these Reports is not possible, and the same applies equally to salvarsan. Therefore, an attempt will be made to present in as objective a form as possible the impression gained from a study of the publications which have appeared during the past year. In the first place, it must be placed on record that the introduction of neosalvarsan, compared with salvarsan, was fully justified, although not all the authors who report on the use of the drug are agreed that it marks an advance. Certainly the ready solubility of neosalvarsan constitutes a marked simplification in technique in comparison with the more complicated preparation of a solution of salvarsan. However, caution is necessary in using solutions of neosalvarsan; in the first place, care must be taken to employ only fresh solutions (which have not been heated), since neosalvarsan is a very sensitive preparation. It is superfluous to add that the greatest attention must be paid to the distilled water used for preparing the solutions ("water-error"). The technique, too, must be faultless.

With regard to the toxicity of neosalvarsan, it is now generally recognized to be less toxic than salvarsan. However, whether it is for this reason better suited than salvarsan for the treatment of out-patients appears to me to be still undecided. Further, the use of large doses seems to have been generally abandoned in favour of smaller amounts, although the latter are less effective, for it is quite possible, if not probable, that the severe intoxications observed, or the deaths reported, were due to an overdose of the drug. In addition, in giving repeated injections the question must be taken into account whether neosalvarsan really has a cumulative action, as has been recently asserted, since this would be a drawback compared with salvarsan. Recently greater value has been laid upon the use of a more concentrated solution of neosalvarsan. Not only is it possible to exclude in a large measure the "water-error", but with its use a marked effect on the spirochætes and on the Wassermann reaction is produced. The use of concentrated solutions is based upon Ravaut's

Ravaut, Presse médicale 1913, No. 18, p. 171. — Münchener medizinische Wochenschrift 1913, No. 20, p. 1126. — Berliner klinische Wochenschrift 1913, No. 22, p. 1031.

observation that owing to the slow rate of infusion of dilute solutions they are in part oxidised and consequently may favour the occurrence of unpleasant side-effects. This question has been dealt with, *inter alia*, by C. Stern, Th. Katz, R. Frühwald, A. Bayet, D. Gurari and W. Fatjanow. Gurari first established by experiments on animals that the use of concentrated solutions was free from danger, and then undertook trials in man, gradually increasing the concentration of the solution employed from 1 in 50 to 2 in 50. The intravenous injection of this concentration was very well borne; the author gave 0.3 to 0.4 gramme of neosalvarsan for a single dose. Bayet, too, expresses himself satisfied with the results obtained by this method. In fresh, untreated cases of syphilis Katz injected 0.3 to 0.6 gramme of neosalvarsan in 10 c. c. of water, and in every case he found that the spirochaetes had disappeared by the following day. The action displayed by these injections is equal to that of salvarsan. Frühwald came to the following conclusions: Three injections of 0.6 gramme of neosalvarsan in 10 c. c. of water, given in the course of ten days, display a prompt effect on the syphilitic manifestations in all stages and cause their disappearance in about two weeks' time. After the first injection secondary effects such as fever, headache, vomiting and diarrhoea occur in about 66 p.c. of the cases. Patients with extensive, active syphilitic manifestations are especially affected. After the second injection these by-effects are considerably rarer, but occur somewhat more frequently after the third injection. Cutaneous reactions such as early or late erythematata are frequently seen. Scrupulous care should be taken to avoid infiltrations due to the solution passing into the subcutaneous tissue. If these do occur they are harmless to the function of the arm if appropriate treatment is adopted. No serious injury referable to the use of the concentrated solution was observed.

Wechselmann's investigations have led to an impor-

Stern, *Münchener medizinische Wochenschrift* 1913, No. 13, p. 691.

Katz, *Münchener medizinische Wochenschrift* 1913, No. 42, p. 2337.

Frühwald, *Münchener medizinische Wochenschrift* 1913, No. 45, p. 2512.

Bayet, *Journal médical de Bruxelles* 1913, No. 25, p. 238.

Gurari-Fatjanow, *Wratschebnaja Gazeta* 1913, No. 14.

Wechselmann, *Münchener medizinische Wochenschrift* 1913, No. 24, p. 1309.

tant innovation in the technique of neosalvarsan injections. This investigator found that the preparation may be injected subcutaneously, although this mode of exhibition had been deprecated owing to the fear of infiltrations. The technique requires special care, and the author states that it is more difficult than intravenous injection. The injection must not be made into the loose cellular tissue nor into the wall of a vein, but must be made only into the hollow space between the fat and fascia, as here it does not cause any painful reaction. According to Wechselsmann it is easy to ascertain whether the point of the needle has been properly introduced. "If the point of the needle lies exactly on the fascia and the lumen is not closed by a connective tissue trabecula, on carefully injecting the solution a portion flows back. Therefore, before injecting the solution of salvarsan I always ascertain whether the needle lies in a proper position by first injecting 0.7 p. c. solution of sodium chloride. If an easily worked Record syringe is used, the absence of any force required in emptying the syringe proves that the injection is being made into a lumen, whereas an appreciable amount of opposition is felt on infiltrating the tissue. Whoever wishes correctly to make subcutaneous injections must have had sufficient practice to enable him to feel these differences with certainty". Wechselsmann injected 0.1 to 0.9 gramme of neosalvarsan in 1 c. c. of physiological salt solution. He states that a solution of 0.1 gramme in 1 c.c. of saline solution, given in doses of about 3 c. c., is apparently best tolerated.

Wechselsmann's findings are confirmed by J. Fabry. He states that subcutaneous injections display a slower, but more lasting action. They cannot replace intravenous injection, but in suitable cases may supplement the latter.

The use of neosalvarsan in gonorrhœa and in amoebic dysentery is new; whether it holds out a promise of success cannot be decided at present in view of the scanty data available. J. Janet and Lévy-Bing have tried it in gonorrhœa and its complications and they found that the local application of a 2 p. c. solution of neosalvarsan in gonorrhœa of the urethra, or of the vagina and portio, caused the rapid disappearance of the gonococci. Injections of a freshly

Fabry, Medizinische Klinik 1913, No. 33, p. 1334.

Janet and Lévy-Bing, Gazette des hôpitaux 1913, No. 21.

prepared solution of neosalvarsan are given, or tampons impregnated with the solution are applied. As has been already reported by other authors, neosalvarsan is especially effective in cases in which both syphilis and gonorrhœa are present, in which the intravenous injection of the preparation is indicated. This also applies to the treatment of amœbic dysentery, in which it was successfully employed by S. H. Wadhams and E. C. Hill in three cases. On the other hand, P. Cohn, E. Bachstetz and H. Hoehl report that the local use of neosalvarsan in keratitis parenchymatosa proved ineffective. Igersheimer also states that it gave negative results.

Reference may be made to the following publications:

Syphilis and Spirochaetosis:

Touton, Berliner klinische Wochenschrift 1913, No. 11, p. 484.
— Lier, Wiener klinische Wochenschrift 1913, No. 11, p. 410. —
Gerber, Münchener medizinische Wochenschrift 1913, No. 12, p. 634. —
Gutmann, Berliner klinische Wochenschrift 1913, No. 13, p. 581. —
Leredde, Bulletin de la société de Dermatologie 1912, p. 437. —
Wolff, Berliner klinische Wochenschrift 1913, No. 19, p. 879. —
Bayet, Journal médicale de Bruxelles 1912, No. 47. —
Marinesco, Zeitschrift für physikalische und diätetische Therapie 1913, April; Berliner klinische Wochenschrift 1913, No. 16, p. 744. —
Solowieff, Dermatologische Wochenschrift 1913, No. 21, p. 596. —
Grünberg, Petersburger medizinische Wochenschrift 1913, No. 15, p. 177. —
Marschalko, Orvosi Hetilap 1912, No. 33. —
Sabsowitsch, Wratschebnaja Gazeta 1913, No. 4, p. 133. —
Freund, Prager medizinische Wochenschrift 1913, No. 12, p. 161. —
Fabry, Medizinische Klinik 1913, No. 34. —
Lévy-Bing, Gazette des hôpitaux 1913, No. 21. —
Gibbard-Harrison-Cane, Journal of the Royal Army Medical Corps 1912, No. 19, p. 291. —
Kleipot, Nederlandsch Tijdschrift voor Geneeskunde 1913, I, p. 851. —
Poltio, Gazzetta degli ospedali 1913, No. 76. —
Schäfer, Deutsches Archiv für klinische Medizin, Vol. 108, No. 5—6.

Malaria:

Baetge, Münchener medizinische Wochenschrift 1913, No. 42, p. 2379 and No. 50, p. 2776. —
Iwanow, Wratschebnaja Gazeta 1912, No. 47.

Granuloma:

Sabella, II Policlinico 1913, No. 5.

Wadhams-Hill, Journal of the American Medical Association, August 9, 1913. —
Semaine médicale 1913, No. 44, p. 522.

Cohn, Wochenschrift für Therapie und Hygiene des Auges 1913, No. 20, p. 161.

Bachstetz, Wiener klinische Wochenschrift 1913, No. 3, p. 101.

Hoehl, Münchener medizinische Wochenschrift 1913, No. 2, p. 72.

Igersheimer, Medizinische Klinik 1913, No. 10, p. 389.

Dosage:

Neumayer, Münchener medizinische Wochenschrift 1913, No. 48, p. 2672.

Technique:

Dreyfus, Münchener medizinische Wochenschrift 1913, No. 12, p. 630. — Duhot, ibidem 1913, No. 20, p. 1088. — Dersca, ibidem 1913, No. 29, p. 1601. — Zumbusch, Wiener klinische Wochenschrift 1913, No. 32, p. 1205. — Kerl, ibidem 1913, No. 50, p. 2076.

Secondary Effects:

Wahle, Münchener medizinische Wochenschrift 1913, No. 7, p. 354. — Escaude, Gazette des hôpitaux 1913, No. 12. — Robertson, Journal of American Medical Association November 8, 1913.

Deaths:

Leredde, Dermatologische Wochenschrift 1913, No. 11, p. 321. — Goureau, ibidem 1913, No. 11, p. 323. — Carle, Medizinische Klinik 1913, No. 48, p. 1993.

Veterinary Medicine (Pneumonia):

Stödter, Berliner tierärztliche Wochenschrift 1913, No. 11, p. 195. — Fontaine, Zeitschrift für Veterinärkunde 1913, No. 11, p. 472. — Schwerdt, ibidem 1913, No. 11, p. 476.

Nitroso- β -Naphthol.

α -nitroso- β -naphthol, $C_{10}H_6(NO)OH$, forms orange-brown crystals which are soluble in ether, alcohol, benzol and glacial acetic acid. Melting point $109^{\circ}C$. It is practically insoluble in water.

Knorre and some other authors have used this preparation in analytical work to detect and precipitate various metals, such as iron, cobalt and copper. In a recent communication W. Schmidt states that it may be used as a precipitant for the platinum metals, since it only precipitates palladium. For this purpose a saturated solution of the preparation in 50 p. c. glacial acetic acid is employed. The addition of this reagent to a solution of palladium produces a bulky reddish-brown precipitate, which is readily filtered and washed. This reaction is perceptible in 1 c. c. of a solution containing 1 gramme of palladium and ammonium chloride in 1 000 000 parts, from which it is apparent that the method may be used quantitatively. Other salts of metals of the platinum group do not react in the same way with nitroso- β -naphthol, and

Knorre, Merck's Reagenzien-Verzeichnis 1913, p. 192.

Schmidt, Zeitschrift für anorganische Chemie 1913, Vol. 80, p. 335.

even small amounts of palladium may be estimated in the presence of large amounts of platinum. The palladium-nitroso- β -naphthol compound has the composition $C_{10}H_6NO_2$ -Pd- $C_{10}H_6NO_2$. On ignition it yields pure palladium, which is weighed as metal.

Noviform.

M. Käsbohrer, F. Schmidt, Molnár Béla and W. Speck are agreed that noviform* is an efficient antiseptic for wounds, and employed in the shape of dusting powder, bougies, 10 p. c. gauze, ointment, or emulsion with olive oil, is useful in the treatment of wounds, burns, fistulas, furuncles, whitlows, phlegmons, abscesses and carbuncles. It has a marked action in limiting secretion, acts as a deodorant and stimulates granulation, without causing any local or general harm whatever. Hence it can be used with advantage as a substitute for iodoform in cases of idiosyncrasy to the latter. R. Patek used it with gratifying results in gynæcological cases, such as leucorrhœa, in the form of insufflations, either per se or mixed with kaolin and talc. Although the author failed to observe any marked advantages over the customary exsiccant dusting powders, he believes that it had a curative effect in erosions of the portio. Insufflations of noviform never caused smarting or redness of the mucous membranes. The use of this remedy also proved successful in ulcers of the vagina due to pressure, such as occasionally occur in wearing a pessary.

Noviform appears to have awakened special interest in ophthalmology, and its use in eye work is reported upon by W. Clausen, G. Freytag, M. Gstettner, H. Adler,

Käsbohrer, Münchener medizinische Wochenschrift 1913, No. 44, p. 2455.

Schmidt, Prager medizinische Wochenschrift 1913, No. 44.

Béla, Wiener medizinische Zeitung 1913, No. 16. — Deutsche Medizinalzeitung 1913, p. 593.

Speck, Münchener medizinische Wochenschrift 1913, No. 34, p. 1881.

* Compare Merck's Report 1912, p. 306.

Patek, Deutsche medizinische Wochenschrift 1913, p. 1204.

Clausen, Wochenschrift für Therapie und Hygiene des Auges 1913, Vol. 16, No. 33, p. 272.

Freytag, Berliner klinische Wochenschrift 1913, No. 27, p. 1261.

Gstettner, Wiener medizinische Wochenschrift 1913, No. 23.

Adler, Wochenschrift für Therapie und Hygiene des Auges 1913, Vol. 17, No. 8, p. 63.

Klages, R. Rauch and Haass. On account of its properties, described in the foregoing, Clausen used noviform in the form of an ointment in squamous and ulcerous blepharitis, with satisfactory results. The ointment also proved useful in erosions of the cornea and after the removal of foreign bodies from the cornea. This is confirmed by Rauch, who prefers a 1 or 2 p. c. noviform ointment as an antiseptic to the use of the preparation as a powder. It is also indicated in corneal and serpiginous ulcers. In the treatment of the latter the author combined the use of noviform with that of a 2 p. c. collargol ointment. In keratoconjunctivitis in the ulcerating stage the author saw good results in several cases, also in blepharitis, in trachoma when on the decline, and in combating streptococci before operations for cataract. He always applied the preparation in ointment form, as he considers the latter preferable for external application to dusting with powder, which is more liable to cause irritation.

Freytag employed ointments containing 2 to 10 p. c. of noviform. In addition to the above-cited indications he also employed the preparation for the treatment of herpes corneæ, and obtained a cure by the prolonged use of a 5 to 10 p. c. ointment. He also used it in the treatment of keratitis interstitialis and scleroticans, episcleritis and scleritis; if necessary, in combination with dionin. On the other hand, in conjunctivitis and keratitis eczematosa noviform did not prove superior to the older remedies, such as calomel and yellow mercuric oxide ointment. Further, he used it in operations on the eyelids and lacrymal sac, and also in abscesses and wounds of the lacrymal sac. It always proved effective, without displaying any harmful side-effects. The other above mentioned authors express themselves in equally favourable terms. It may be mentioned that Haass tried the use of noviform in ophthalmia neonatorum in which it displayed a prompt effect. He used it as an ointment (5 to 10 grammes: 100 grammes of mitin).

F. Schwerdtfeger, G. Dinolt and O. Frese report

Klages, *ibidem* 1913, Vol. 17, No. 8, p. 65.

Rauch, *Berliner klinische Wochenschrift* 1913, No. 47, p. 2189.

Haass, *Wochenschrift für Therapie und Hygiene des Auges* 1913, Vol. 17, No. 10, p. 77.

Schwerdtfeger, *Prager medizinische Wochenschrift* 1913, No. 11.

Dinolt, *Berliner klinische Wochenschrift* 1913, No. 27, p. 1261.

Frese, *Deutsche medizinische Wochenschrift* 1913, No. 36, p. 1733.

on the use of noviform in oto-rhinology. Used as a snuff, it proved effective in acute and chronic nasal catarrhs, while its application in the form of powder or of gauze yielded good results in processes accompanied by fœtor, ulcers of the mouth and throat, operations wounds, etc.

Novocaine.

As is well known, A. Hoffmann found that it was possible considerably to increase the anæsthetic effect of a solution of novocaine (containing suprarenin) by the addition of potassium sulphate, so that the same effect can be obtained by a 0.1 p. c. solution as with a 0.5 p. c. solution of novocaine without potassium sulphate. However, H. Braun states that a 0.1 p. c. solution of novocaine may prove effective, but its anæsthetic effect is by no means reliable. He therefore considers the use of dilute solutions of novocaine (and suprarenin), as advocated by Hoffmann, to be a step backward, but he is in favour of the addition of potassium sulphate to solutions of the strength hitherto employed. He is of opinion that the intensified action of novocaine solution produced by the addition of potassium sulphate should not be used to depreciate the results hitherto obtained, but to improve them and render them more reliable. In those cases in which unduly large amounts of novocaine would have to be used, the strength of the solution may be decreased, but not below a content of 0.25 p. c. In this case the content of suprarenin must be increased to that ordinarily present in a 0.5 p. c. solution of novocaine. For instance, a stock solution may be prepared containing 4 grammes of novocaine and 0.4 gramme of potassium sulphate in 100 c. c. of water; before use this solution is diluted with a solution of 4 grammes of potassium sulphate and 7 grammes of sodium chloride in 1000 c. c. of water, whereupon the suprarenin is added. Used in this way Braun believes Hoffmann's discovery to mark an advance in local anæsthesia*.

H. Harttung obtained a complete success with Braun's method of inducing anæsthesia by novocaine-suprarenin in an

Hoffmann, Deutsche medizinische Wochenschrift 1912, No. 48. Compare Merck's Report 1912, p. 308 and Zentralblatt für Chirurgie 1913, No. 35.

— Medizinische Klinik 1913, No. 49.

Braun, Zentralblatt für Chirurgie 1913, No. 39.

* Compare Brunner, Zentralblatt für Chirurgie 1913, No. 28.

Harttung, Deutsche medizinische Wochenschrift 1913, No. 10.

operation on the sternum (mediastinotomia longitudinalis Sauerbruch). The patient, a woman, was given 0.01 gramme ($\frac{1}{6}$ grain) of morphine half an hour before the operation. On both sides of the sternum and close to the latter, a little above the middle of each of the first to fifth intercostal spaces a wheal was made, five in all, and from each of these punctures 5 c. c. of a 1 p. c. solution of novocaine-suprarenin was injected into the intercostal space. Thereupon, by connecting all the wheals, the whole area round the field of operation was injected with a 0.5 p. c. solution, whereby the two lowest sites of injection were connected by an obtuse angle opening upwards. The infiltration was also used to anæsthetise the jugulum. The operation was begun twenty minutes later, and was completed without the aid of a narcotic and without the patient uttering a single cry of pain.

R. Langbein states that epidural injections of novocaine are indicated in genuine sciatica when energetic treatment with antineuralgic remedies and the application of warmth have failed. These are as a rule cases of sciatica of the roots, in which injections into the nerve scarcely hold out a promise of success. For epidural injection the author made use of a solution of 1 gramme of novocaine, 0.5 gramme of sodium chloride and 0.25 gramme of sodium bicarbonate (highest purity) in 100 c. c. of water. For particulars of the technique (according to Lâwen) the original paper should be consulted.

Omnopon (Pantopon).

P. Buchmann describes a method of anæsthesia which he found useful in various operations, in appendicectomies, hernias, hæmorrhoids, hydroceles, castrations, cystectomies, rectal fistulas, prolapse of the rectum, etc. As the action of omnopon sets in later than that of morphine, the author adopts the following technique: Two hours before the operation the patient is given a subcutaneous injection of 1.1 c. c. of a 2 p. c. solution of omnopon. Shortly before the operation an injection of 2 to 12 c. c. of a warmed 0.5 p. c. solution of cocaine hydrochloride with one or two drops of adrenalin is made locally. The anæsthesia induced by this method was

Langbein, Deutsche medizinische Wochenschrift 1913, No. 1.

Buchmann, Deutsche medizinische Wochenschrift 1913, No. 49, p. 2403.

almost always sufficient, and in only three cases out of 456 operations it was necessary to resort to the use of chloroform. This method is especially indicated and readily applicable for the purpose of ensuring absolute rest of the intestines after the above mentioned operations. The fact that omnopon anæsthesia lasts longer than that following morphine is an advantage; but as it sets in later it is useless in urgent cases.

In bronchial asthma W. Stadion prescribed omnopon tablets during the period of freedom from attacks and succeeded in preventing the return of the paroxysms, or their recurrence is very considerably delayed. Injections of omnopon proved effective during an attack, and were not followed by vomiting or headaches. The preparation is extremely useful in incoercible vomiting due to gastric disturbances. According to Doebeli, omnopon syrup, i. e., a solution of 0.05 gramme ($\frac{3}{4}$ grain) of omnopon in 100 grammes ($2\frac{2}{3}$ oz) of syrup, may be prescribed for children in the treatment of affections of the respiratory tract, to alleviate pain, and in conditions of excitement, and also to induce sleep. A communication by S. Wolff shows that caution is necessary in administering opiates to children; after giving one dose of 0.1 milligramme of omnopon to a child aged one year he observed severe symptoms of opium poisoning which persisted for a considerable time.

T. Kidodze recommends the use of omnopon for the same purposes for adults in doses of 0.01 to 0.02 gramme ($\frac{1}{6}$ — $\frac{1}{3}$ grain), especially subcutaneously. To relieve distressing cough and as a sedative in hæmoptysis a mixture containing 0.04 to 0.06 gramme ($\frac{2}{3}$ —1 grain) of omnopon in 200 grammes (7 oz) is prescribed; or single doses of 0.005 to 0.01 gramme ($\frac{1}{12}$ — $\frac{1}{6}$ grain) of omnopon. Small repeated doses are useful in tuberculous diarrhœa, but a single large dose is even better.

Reference may be made to a review of the literature on omnopon by R. Weiermiller, in which the author

Stadion, Therapie der Gegenwart 1913, No. 7, p. 335.

Doebeli, Monatsschrift für Kinderheilkunde 1913.

Wolff, Monatsschrift für Kinderheilkunde 1913, Vol. 12, p. 77. —

Therapeutische Monatshefte 1913, No. 12, p. 887.

Kidodze, Dissertation Berne 1913.

Weiermiller, Klinisch-therapeutische Wochenschrift 1913, No. 16, p. 492.

deals exhaustively with the analgesic and narcotic properties of omnopon and its indications.

Organotherapeutic Preparations*.

Adrenalin and Suprarenin**.

H. von Salis reports a case illustrating the value of adrenalin in the treatment of osteomalacia. It was a case of recurrence of osteomalacia in which castration had proved ineffective, whereas daily injections of 0.5 c. c. of adrenalin led to a cure. In eight out of twelve cases R. Marek also obtained complete recovery, or marked improvement, by the use of injections of adrenalin; in one case, it is true, only after castration.

The successful results following the use of adrenalin in the treatment of osteomalacia induced R. Schmidt to try this remedy in arthritic processes, since both maladies offer several points of similarity with respect to predisposition and amenability to therapeutic treatment. He injected subcutaneously 0.5 to 1 c. c. of adrenalin daily into the thigh (with due regard to the well-known contra-indications), and obtained extremely satisfactory results. He states that etiologically dissimilar joint processes, such as polyarthritis acuta vulgaris, arthritis gonorrhoeica and syphilitic forms, react favourably to adrenalin.

Further reports on the treatment of asthma*** by adrenalin have been contributed by G. Keyzer and H. Weyer. Keyzer gave adrenalin by mouth in doses of one tablespoonful every three hours of a mixture of 2.5 grammes of adrenalin and 250 grammes of water, and with this treatment immediate relief was obtained. Weyer obtained the same success by

* Compare Merck's Report 1908.

** In the following article whenever adrenalin or suprarenin is mentioned the 1:1000 solution of either is meant.

Salis, *Münchener medizinische Wochenschrift* 1913, No. 46, p. 2563.

Marek, *Zentralblatt für Gynäkologie* 1913, No. 6, p. 217.

Schmidt, *Medizinische Klinik* 1912, p. 1489. Compare F. Gaisböck,

Wiener klinische Wochenschrift 1913, No. 32, p. 1311 and H.

Januschke, *ibidem* 1913, No. 28, p. 1164.

*** Compare Merck's Report 1912, p. 315.

Keyzer, *Nederlandsch Tijdschrift voor Geneeskunde* 1913, No. 15.
Weyer, *ibidem* 1913, No. 6.

the subcutaneous injection of 0.5 c. c. F. Dumstrey uses suprarenin for the same purpose. Like adrenalin it is an excellent remedy for asthma, but like the former it can be used only under certain conditions. Dumstrey lays stress upon the value of systematic treatment with respiratory exercises, and he gives suprarenin only when the patient loses control of his breathing, and in the shape of injections only in the severest cases. For this reason the patient should not be entrusted with a syringe. Hence suprarenin should be used only in an emergency, to facilitate breathing during an attack, and the patient should breathe as instructed, since suprarenin alone can never by itself achieve a complete cure, while its injudicious and prolonged use may lead to serious harm.

Of special interest is a paper by B. A. Houssay on the combined use of adrenalin and hypophysin, in which the author also refers to the clinical use of this combination. His investigations show that it combines the intensive action of both organic products, i. e., the action of adrenalin on the heart and vessels with the protracted action of hypophysin on the organs. By mixing both in suitable proportions the initial depressant effect of hypophysin may be lessened. This is the case with a mixture of four or five drops of adrenalin and 1 c. c. of hypophysin, to be used for intravenous injection in shock and collapse. The hypophysin increases the action of the relatively poisonous adrenalin, therefore smaller doses of a combination of both display the desired result. Hence its subcutaneous or internal use is successful in fulminating intoxications accompanied by hypotension, in tachycardia and toxic myocarditis. This combination induces more powerful and more lasting local ischæmia than adrenalin per se, and should be worthy of trial in ophthalmological work and in otorhinology. Further, the author points out that adrenalin neutralises the powerful enterokinetic action of hypophysin, while its mydriatic effect is mitigated by the hypophysin.

Mention may be made of a work by L. Hess and J. Wiesel on the influence of adrenalin on acute experimental nephropathies.

Dumstrey, Allgemeine medizinische Zentral-Zeitung 1913, No. 45.

Houssay, Wiener klinische Wochenschrift 1913, No. 13.

Hess-Wiesel, Wiener klinische Wochenschrift 1913, No. 9.

Hormonal.

According to H. Schricker, hormonal displays a prompt and reliable action in most cases of peritoneal and post-operative intestinal paresis, and its effect of stimulating peristalsis is beyond doubt. The author is unable to state whether this is a specific action or whether it is produced in consequence of a fall in blood pressure, but he inclines to the former view. In severe disturbance of the intestinal innervation hormonal fails, or displays only a very slight action. In chronic constipation about 70 p. c. of the cases are benefited. However, in using this preparation it must be borne in mind that it is not so harmless as was at first assumed. Even the new improved hormonal, according to R. Dittler and R. Mohr, still causes lowering of blood pressure, and should therefore be employed with caution. Schricker states that it should be used only in the clinic or hospital, where expert assistance is always at hand, and after the indications for its use have been definitely established. The author states that hormonal is indicated in cases of obstinate constipation which have resisted all other remedies, and in post-operative and reflex intestinal paresis in which the other methods of treatment, especially the application of incandescent light, have failed. The heart's action should at the same time be energetically assisted by the administration of digalen or camphor.

On account of the secondary effects of hormonal F. A. Hesse injected it only in cases of very severe intestinal paresis, practically as a last resort. Nevertheless, his results are worthy of note, for in every case he obtained a positive reaction in that the bowels moved. A single injection of 15 to 20 c. c. ($\frac{1}{2}$ — $\frac{2}{3}$ oz) of hormonal proved sufficient for adults, and the action set in after from five to forty hours. However, its action was always accompanied by a fall in blood pressure, although the latter was, as a rule, insignificant, but in one out of seven cases it necessitated an interruption in the injection and camphor had to be injected. Collapse never occurred. Although hormonal cannot be regarded as harmless, Hesse still maintains that in all his cases in which it was used

Schricker, *Klinisch-therapeutische Wochenschrift* 1913, No. 7, p. 198.
Dittler-Mohr, *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie* 1913, No. 5.

Hesse, *Therapeutische Monatshefte* 1913, No. 10, p. 698.

as a last resort it displayed an excellent effect, and often proved a life-saving procedure.

P. Sarnizyn gave hormonal in some cases intravenously and in others intramuscularly, and in most instances of atonic constipation he obtained the desired result. On the other hand, in spastic constipation and in dilatation of the ampulla of the rectum it displayed no effect whatever.

Güsbeck and Orth tried to paralyze the depressing effect of hormonal on the blood pressure by combining it with adrenalin. They succeeded in causing a rise of blood pressure, which, however, was quickly negated by the influence of hormonal. Adrenalin also proved unsuitable for this purpose, inasmuch as it has an adverse action on the intestinal peristalsis, and the use of strophanthin or pituitrin holds out a greater promise of success. The latter not only raises the blood pressure but also stimulates peristalsis; however, a combination of hormonal and pituitrin for increasing peristalsis is open to criticism owing to the different points of attack of both remedies, and further trials are necessary to elucidate its action. Whether a combination of this kind is required under ordinary circumstances still awaits explanation; P. Sackur states that if the infusion into the vein is made slowly an alarming fall of blood pressure or collapse may be avoided with certainty, even in very debilitated persons. However, at least fifteen minutes should be required to inject a dose of 20 c. c. ($\frac{2}{3}$ oz). Hormonal is indicated in paralytic (dynamic) ileus, post-operative intestinal paresis, and simple atonic constipation. It is ineffective in spastic constipation and mechanical ileus. In recalcitrant cases further experience is necessary to establish whether the dose should be increased to 30 or 40 c. c. ($1\frac{1}{3}$ oz), or whether the infusion should be repeated. As a precautionary measure the author advises the use of a burette such as is employed for salvarsan injections, in the place of a syringe. H. L. Richartz thinks it advisable to confine the patients to bed after making the infusion, since it is usually followed by more or less severe rigors, and the

Sarnizyn, Russkij Wratsch 1913, No. 36.

Güsbeck-Orth, Zentralblatt für die gesamte Chirurgie 1913, Vol. 1, p. 748. Compare Schlaginweit, Zentralblatt für die gesamte innere Medizin 1913, Vol. 7, p. 574.

Sackur, Deutsche medizinische Wochenschrift 1913, No. 9, p. 401.

Richartz, Deutsche medizinische Wochenschrift 1913, No 22, p. 1057.

first evacuation should be assisted by the administration of castor oil.

B. Burianek gave hormonal in six cases of post-operative ileus in doses of 20 c. c. ($\frac{2}{3}$ oz), intravenously or intramuscularly. It was injected intramuscularly in two cases: in one the effect showed itself only after forty-eight hours, and in the other it failed. The intravenous injection also yielded a negative result in one case. In three other cases it which it was given intravenously the bowels moved on the following day after giving an enema; in the second case slight collapse was observed, and in the third severe collapse occurred immediately after the injection and the patient died from asphyxia.

These unpleasant experiences might easily be avoided if the investigations undertaken by H. J. Achard are confirmed. The author found that following the oral administration of 20 c. c. ($\frac{2}{3}$ oz) of hormonal to patients suffering from chronic constipation the bowels moved regularly for several months.

Ovarian Preparations.

For obvious reasons only animal organs and preparations made from these are available for organotherapy, although it is probable that, apart from specific differences, the human organs contain more powerful hormones. Recasens undertook experiments with human ovaries and with extracts prepared from these. The author used an ovarian extract from young women who had been operated on for myomata, on the assumption that it would display an increased internal secretory action. It was sterilized and put up in ampoules. In seven cases doses of 1 to 2 c. c. were injected subcutaneously every third day. In two cases of amenorrhœa a cure was effected by this treatment, while two cases derived no benefit. Three cases of dysmenorrhœa and oligomenorrhœa were cured; in one of these conception took place later. Apart from the fact that no definite conclusion can be drawn as to the value of this treatment in view of the small number of cases treated with human ovarian extract, further trials would have to be undertaken with therapeutic material resembling that em-

Burianek, *Casopis lekaruv ceskych* 1913, p. 540.

Achard, *American Medicine* 1913, Vol. 19, p. 111.

Recasens, *Münchener medizinische Wochenschrift* 1913, No. 36, p. 2021.

ployed by the author. However, it may be assumed that an animal extract will yield similar results.

J. Hirsch used a preparation of this kind, and 2.2 c. c. of his preparation, called glanduovin, represent 2 grammes of ovarian substance. It is supplied in sterile ampoules and is injected subcutaneously. The following results have been obtained:

1. In 25 out of 28 cases glanduovin exerted a beneficial influence on disturbances at the menopause both natural and artificially induced;

2. Dysmenorrhœic troubles due to hypofunction of the ovaries were usually cured, i. e., in 32 out of 37 cases;

3. This treatment failed in intra-menstrual pain (Mittelschmerz);

4. In ologomenorrhœa and amenorrhœa one failure was observed among 16 cases;

5. In two cases of dermatoses in pregnancy only one was beneficially influenced;

6. In two cases of pruritus vulvæ in pregnant women a success was obtained, as well as in a case of pruritus in a non-pregnant woman;

7. An improvement in hyperemesis gravidarum was only occasionally observed (in 9 out of 19 cases);

The injections were repeated daily until an improvement was manifest; usually two or three injections were required. To explain the action of the preparation the author assumes that the hormone introduced reinforces the patient's own hormone.

In addition to those ovarian preparations* which are prepared by drying ovaries, I now also supply a water-soluble ovarian preparation in tablets. The results hitherto obtained show that owing to its ready absorption it is an efficient organic preparation, the use of which holds out a promise of success in the indications for ovarian therapy, especially in disturbances at the menopause.

Parathyroid Gland.

O. Meyer relates a case of spasmodophilia in which he adopted parathyroid treatment. It was that of a child, aged

Hirsch, Berliner klinische Wochenschrift 1913, No. 39, p. 1319.

* Compare Merck's Index 1910, p. 208.

Meyer, Therapie der Gegenwart 1913, No. 8, p. 354.

2 $\frac{1}{4}$ years, which had already for a long time received the most careful dietetic and medicinal treatment, without being relieved of the laryngospasms and carpopedal spasms. After some time whooping cough developed, associated with eclamptic fits. The whooping cough was cured but the spasmophilia remained, and resisted the administration of phosphorated cod-liver oil, sodium phosphate and calcium bromide. The author decided to try parathyroid therapy, and prescribed one tablet of parathyroidin three times daily (1 tablet = 0.1 gramme of parathyroid gland). The first success was apparent after eight days in that the carpopedal spasms remained absent. After two and a half weeks diarrhoea occurred, which was stopped by giving three times a day one-tenth of a drop of tincture of opium, and by not giving any sugar or vegetables for one day. Later, diarrhoea again occurred occasionally, which the author ascribes to the parathyroid treatment. At first 75 tablets were given and the result of this treatment showed itself in the gain in weight, and the disappearance of the laryngospasms and carpopedal spasms, whereas the fascialis phenomenon and the hyper-excitability of motor nerves to galvanic stimulation remained unchanged. This treatment was continued with interruptions, and led to a complete cure. According to Meyer, this successful result was unquestionably due to parathyroid treatment, but the author refrains from drawing any definite conclusion as to its therapeutic value, since the same treatment failed in another similar case.

Pituitary Preparations. (Glanduitrin, Hypophysin, Pituglandol, Pituitrin.)

How far the various preparations of the pituitary gland* at present on the market exhibit the same pharmacological or physiological action cannot for the present be discussed here. M. Guggenheim believes that the characteristic action of pituitary extracts is not attributable to one single, but to several substances. His investigations show that a number of active principles are present, all of which belong to the group of proteinogenic amines, which includes substances formed from known or unknown amino-acids by the loss of a carboxyl group, e. g., β -iminazolyethylamine (histamine) from

* Compare Merck's Report 1912.

Guggenheim, Medizinische Klinik 1913, No. 19, p. 755.

histidine, indoethylamine (tryptamine) from tryptophan, and adrenalin derived from a hypothetical amino-acid. H. Fühner has made an exhaustive study of the substances present in the pituitary gland, and he states that in pituitary extract free from albumin (prepared from the infundibular portion) eight different substances are present, of which four participate in the intense action displayed on the uterus. These four substances can be isolated in the form of their sulphates as a chemically pure, crystalline preparation of constant composition, which is issued under the name of hypophysin as a 1:1000 solution. 1 c. c. contains 1 milligramme of hypophysin and exhibits the same behaviour as a pituitary extract of which 1 c. c. is equivalent to 0.2 gramme of fresh gland. This preparation displays the entire action of pituitary extract on the uterus, blood pressure and respiration. The physiological aspect of this action is dealt with in a work by A. F. Fröhlich and E. P. Pick.

According to L. Popielski the therapeutically used pituitary preparations may be divided into preparations which raise the blood pressure (pituitrin, pituglandol), and preparations which lower the blood pressure (hypophysin). The author does not believe that Fühner's pituitary substance is the active principle of the pituitary gland and regards it as an admixture to the latter. In addition, he states that commercial preparations of the pituitary gland vary greatly with regard to their action on the blood pressure, and he found that pituglandol lowers the blood pressure. This effect has certainly no connexion with its oxytocic action, as was also pointed out by other authors (see below).

G. Schickele deals with the question of the difference in action between both portions of the pituitary gland, the posterior and anterior lobes. Whereas it had been hitherto assumed that only the posterior lobe of the pituitary body, the infundibular portion, caused a rise in blood pressure, the author states that under certain conditions pressor substances can be isolated also from the anterior lobe, and,

Fühner, Deutsche medizinische Wochenschrift 1913, No. 11, p. 491.
Fröhlich-Pick, Archiv für experimentelle Pathologie 1913, Vol. 75, p. 92.

Popielski, Berliner klinische Wochenschrift 1913, No. 25, p. 1156.
Schickele, Zeitschrift für die gesamte experimentelle Medizin 1913, No. 6, p. 545.

further, that the extracts prepared from both portions have a diuretic effect. Moreover, he found that the action of the extracts on the uterus is not confined to the substance which influences the blood pressure.

Up to the present pituitary preparations have been chiefly employed in obstetrics and gynæcology, and as their uses in both branches of medicine have already been dealt with, for further particulars the following papers should be consulted:

- Alcober, *La cronica medica de Valencia*, February 10, 1913.
Basset, *Medizinische Klinik* 1913, No. 12, p. 457.
Bergh, *Tidskrift for den norske lægeforening* 1912, p. 1033.
Bosse, *Deutsche medizinische Wochenschrift* 1913, No. 36, p. 1731.
Degollada, *Revista de ciencias medicas de Barcelona* 1913, p. 191;
 Revue de thérapeutique 1913, p. 357.
Espeut, *Münchener medizinische Wochenschrift* 1913, No. 32, p. 1774.
Foges, *Archiv für Gynäkologie*, Vol. 99, No. 3.
Fühner, *Therapeutische Monatshefte* 1913, No. 3, p. 202.
Gall, *Zentralblatt für Gynäkologie* 1913, No. 10, p. 334.
Gisel, *ibidem* 1913, No. 5, p. 167.
Grumann, *Münchener medizinische Wochenschrift* 1913, No. 26, p. 1436.
Herz, *Zentralblatt für Gynäkologie* 1913, No. 20, p. 722 and No. 41.
 p. 1536. — *Semaine médicale* 1913, No. 26, p. 308.
Humpstone, *Zentralblatt für Gynäkologie* 1913, No. 1, p. 43.
Jacoby, *Zentralblatt für die gesamte Therapie* 1913, No. 1, p. 1.
Kratochvil, *Casopis lekaruv ceskych* 1912, No. 32.
Liepmann, *Zentralblatt für Gynäkologie* 1913, No. 21, p. 764.
Lieven, *ibidem* 1913, No. 10, p. 337.
Malinowsky, *ibidem* 1912, No. 43, p. 1425.
Mátyás, *Medizinische Klinik* 1913, No. 29, p. 1164.
Milne, *Indian Medical Gazette* 1913, Vol. 48, p. 225.
Mory, *Deutsche medizinische Wochenschrift* 1913, No. 43, p. 2120.
 — *Allgemeine medizinische Zentral-Zeitung* 1913, No. 45, p. 535.
Neuwirth, *Münchener medizinische Wochenschrift* 1913, No. 38, p. 2120.
Nowikow, *Wratschebnaja Gazeta* 1912, No. 22.
Pachner, *Casopis lekaruv ceskych* 1913, No. 7.
Popandopulo, *Wratschebnaja Gazeta* 1912, No. 36.
Raab, *ibidem* 1912, No. 51.
Rübsamen, *Zentralblatt für Gynäkologie* 1913, No. 21, p. 774.
Schirokow, *Deutsche Ärzte-Zeitung* 1913, No. 9, p. 129.
Senge, *Deutsche medizinische Wochenschrift* 1913, No. 38, p. 1833.
Stolper, *Zentralblatt für Gynäkologie* 1913, No. 5, p. 162.
Tiger, *Wratschebnaja Gazeta* 1912, No. 31.
Vogelsberger, *Deutsche medizinische Wochenschrift* 1913, No. 10,
 p. 487. — *Medizinische Klinik* 1913, No. 16, p. 620.
Vogt, *Deutsche medizinische Wochenschrift* 1913, No. 49, p. 2401.
Wolf, *ibidem* 1913, No. 32, p. 1557.

On the whole, the results of the investigations of these authors are in agreement with the findings published in my last year's Report, and also with the findings of S. Herzberg, who came to the following conclusions as a result of his investigation of hypophysin:

Hypophysin displays a favourable influence on weak and irregular uterine contractions, without causing spasmodic labour pains nor permanent contraction. It is a harmless ecboic which acts in every stage of parturition and does not cause any marked secondary hæmorrhage. The administration of hypophysin succeeded in promptly bringing on labour in postponed labour, at the completion of pregnancy, and one week before the calculated termination of pregnancy, and the duration of labour was not longer than is normally the case. On the other hand, he found it impossible to induce labour several weeks before the end of pregnancy, although it was possible to bring on labour pains. In combination with metreurysis in two cases of placenta prævia the labour pains set in a few minutes after injecting hypophysin. The metreurynter, which was filled with 500 c. c. of fluid, was expelled after scarcely three hours, and version and extraction, which were immediately performed, were successfully carried out. It immediately produced contractions even in extremely severe cases of atony of the uterus in which the use of preparations of ergot had partly failed. In these cases the injection was made directly into the body of the uterus through the abdominal walls. In Caesarian section hypophysin hastens the expulsion of the placenta in the same way as other pituitary preparations, and reduces the loss of blood consequent on operations. According to Herzberg hypophysin is free from undesirable secondary effects.

The above mentioned action of pituitary preparations on the blood pressure induced Klotz to try the use of pituitrin for the purpose of directly combating lowered blood pressure. This preparation certainly promises to be useful in cases of lowered blood pressure due to dilatation of the vessels in the splanchnic region, but it is not indicated in lowering of blood pressure due to primary failure of the heart. In collapse consequent on acute loss of blood, surgical

shock, after medicinal treatment, and especially in toxic fall of blood pressure, pituitrin is extremely valuable. The author's observations are based on fifty injections in cases of peritonitis; however, trials in diphtheria and pneumonia appear justified.

There is probably a connexion between the effect of pituitrin on the vessels and its action on bleeding; E. Rist believes that it is due to constriction of the pulmonary vessels. He succeeded in ten cases of hæmoptysis in immediately arresting the bleeding by an intravenous injection of 0.5 c. c. of pituitrin.

In bleeding in the region of the respiratory apparatus M. Säng er made use of the endonasal application of pituglandol, and he states that in these cases it acts as promptly as its subcutaneous injection. In combination with stypticin cotton wool pituglandol sprays displayed a surprisingly prompt effect in spontaneous and post-operative bleeding from the nose; the hæmostatic properties of stypticin assist the action of the pituitary gland preparation. The endonasal application of the remedy is said to afford prompt relief in asthma and in very profuse menses.

E. Herz, G. A. Wagner and R. Hofstätter report on the secondary effects of, and the injuries due to, the use of pituitary gland preparations. Herz reports that in a primipara with a rachitic pelvis who had been given an injection of 1 c. c. of pituitrin in the first stage of labour in order to shorten the duration of labour, the cervix was entirely torn off from the uterine wall (colporrhexis). The preparation likewise had a deleterious effect on the child which was born in deep asphyxia. F. Spaeth also describes a case in which after two doses of 0.5 c. c. of pituitrin the child was born asphyxiated. He thinks that a remedy which acts so quickly is bound to pass through the placenta into the

Rist, Bulletin et mémoires de la société médicale des hôpitaux 1913, p. 776. — Presse médicale 1913, No. 31, p. 309.

Säng er, Therapeutische Monatshefte 1913, No. 9, p. 644.

Herz, Zentralblatt für Gynäkologie 1913, No. 20, p. 720.

Wagner, Münchener medizinische Wochenschrift 1913, No. 41, p. 2308.

Hofstätter, Deutsche medizinische Wochenschrift 1913, No. 49, p. 2427.

Spaeth, Zentralblatt für Gynäkologie 1913, No. 5, p. 165.

circulation of the child and produce more or less severe intoxication. A case reported by F. Lieven in which 1 c.c. of pituglandol was injected subcutaneously shows that the use of pituitary gland preparations may cause asphyxiation of the child and therefore cannot be regarded as absolutely harmless. Wagner expresses himself in similar terms, as he observed the occurrence of a very severe stenocardiac attack which lasted for hours after an injection of glanduitrin. In this case, in his opinion, this effect was probably due to an abnormal increase of the vaso-constrictor action of the preparation of pituitary gland by reason of individual susceptibility. He therefore warns against the use of pituitary gland preparations in diseases of the coronary arteries and of the cardiac muscle. He also considers that they are by no means devoid of danger in eclampsia, since they may provoke tempestuous labour*. Hofstätter has made an exhaustive study of the failures and injuries observed with pituitary therapy, and he comes to the conclusion that most of the unwelcome experiences, apart from those due to an overdose, are of a nervous nature or may be ascribed to the rise of blood pressure. Many of these are merely chance or wrongly interpreted sequelæ of pre-existing disease. Nevertheless, he also urges caution in uncompensated cardiac defects, advanced arterio-sclerosis and in nervous individuals. In the author's experience a deleterious effect on the kidneys need be feared only in the case of an overdose. However, attention must be drawn to a statement by R. von den Velden who in trials on man saw effects which are at variance with the data obtained by experiments on animals. He found that both with healthy and diseased kidneys the injection of pituitary gland causes no increase, but on the contrary a decrease in the secretion of urine. In view of this finding it would not be out of place to test the renal function before injecting a preparation of pituitary gland, although in normal cases no severe damage to the kidneys need be apprehended, as far as has been observed in practice. A case of idiopathic diabetes insipidus affords an illustration of the influence of pituitary gland therapy on the renal function, in which the

Lieven, *ibidem* 1913, No. 10, p. 337.

* See below: Schlossberger.

Velden, *Berliner klinische Wochenschrift* 1913, No. 45, p. 2083.

injections produced the following surprising result: "Under the influence of injections of pituitrin, and also of hypophysin, but in a less degree by the internal administration of pituglandol, the diabetes insipidus kidney acquires the power of temporarily excreting a urine which is two or three times as concentrated as before; or this may be expressed as a diminution of the excretion of water." It is still an open question whether this finding is of therapeutic importance.

In those cases of eclampsia in which conservative treatment is indicated A. Schlossberger advises a trial with pituitary extract, for the purpose of definitely establishing whether this treatment really ensures so striking a result as he was able to observe in two cases. After giving two injections of 1.1 c. c. of pituglandol (and 0.02 gramme [$\frac{1}{3}$ grain] of omnopon) the attacks ceased after half an hour and three quarters of an hour respectively. In one case, at the end of normal pregnancy, labour passed off normally; in another case, in the sixth month of pregnancy, the foetus was born alive and the placenta was expelled almost at the same time (the foetus died after fifteen minutes). After eight days the patient had completely recovered.

The effect of pituitary gland of stimulating peristalsis, which has already been mentioned*, appears to be gaining in importance in the treatment of constipation, as appears from a paper by G. Katsch. He states that as a rule the movements of the intestine are powerfully stimulated by pituitary extract. The results obtained in practice by B. Houssay and J. Beruti are in agreement with this observation. Especially in paralytic ileus and peritonitis the effect was remarkable. The authors employed a pituitary extract of which 1 c. c. represented 0.2 gramme of posterior lobe; they usually injected 3 c. c.

These authors state that adrenalin abolishes the action of pituitary extract, and therefore should not be used simul-

Schlossberger, Deutsche medizinische Wochenschrift 1913, No. 22, p. 1046.

* Compare Klotz, Merck's Report 1912, p. 328.

Katsch, Zeitschrift für experimentelle Pathologie 1913, Vol. 12, p. 277.

Houssay, Revista de la sociedad medica Argentina 1913, Vol. 21, p. 245.

taneously with the latter. R. Klotz tried the internal use of hypophysochrom, a dye obtained from the pituitary gland, in the treatment of rickets, and he states that this substance acts as a stimulant to the pituitary gland, which controls phosphorus metabolism, and is capable of partly inhibiting its sub-function. He obtained very satisfactory results. After five to six weeks' administration of hypophysochrom tablets all the children treated, several of whom had received no benefit from other remedies, were able to walk; at the same time they showed a decided mental improvement and a gain in weight. This finding is confirmed by K. Weiss, who gave to children under one year three or four tablets daily, to children over one year four or five tablets, and to those over eighteen months six tablets.

H. Hötzel reports on the use of glanduitrin in veterinary practice. He gave to cows 4.4 c. c. and, if necessary, after ten or fifteen minutes increased this amount to 12 c. c., without observing any unpleasant secondary effects. It is useful in primary and secondary atony of the uterus, and can also be employed to arrest bleeding in wounds of the mucous membrane of the uterus.

Spleen.

The action of spleen on malignant tumours is discussed in a work by P. Biach and O. Weltmann. The results reported do not permit of any conclusions as to the therapeutic use of splenic opotherapy in carcinoma, but they afford several facts of interest to organotherapy. The trials undertaken by the authors on rat sarcoma show that the adhesion and power of proliferating of a sarcoma "simultaneously" inoculated with splenic tissue is impaired at the sites of injection through the emulsion of spleen. Through absorption of tumour cells a general immunity is developed, which is enhanced by the emulsion of spleen. Further, the sarcoma-spleen exhibits a far greater inhibitory effect than normal spleen. This inhibitory effect of spleen is based upon an increase of the natural inhibitory power and on the content

Klotz, Münchener medizinische Wochenschrift 1913, No. 21, p. 1145.

Weiss, Therapeutische Monatshefte 1913, No. 7, p. 490.

Hötzel, Allatorvorsi lapok 1913, No. 25.

Biach-Weltmann, Wiener klinische Wochenschrift 1913, No. 27, p. 1115.

of specific substances which have a destructive action on tumour cells. The fact is particularly interesting that animals which have remained free from tumours by the simultaneous injection of emulsion of spleen and tumour still remain immune on re-injecting larger doses. In an investigation of rat-sarcoma E. G. Oser and E. E. Pribram also came to the conclusion that the spleen plays an important rôle in malignant tumours in the organism. They found that in rats deprived of their spleens the tumours grew more rapidly, and that injections of splenic emulsion caused involution or cessation of growth of the tumours. It may be assumed that the spleen provides the body with substances (resembling the antibodies) which are not present in the blood. The splenic emulsion should not be injected directly into the tumour.

The use of preparations of spleen in tuberculosis has already yielded noteworthy therapeutic results*. H. R. Harrower ascribes the benefit resulting from splenic medication to a substance present in spleen which arrests the growth of tubercle bacilli. In addition, spleen exerts a beneficial influence on phagocytosis, pancreatic digestion, the formation of enterokinase and of hæmoglobin, and on the development of connective tissue.

Thymus Gland.

The recent investigations of K. Basch furnish a confirmatory physiological basis for the therapeutic use of the thymus gland, which was exhaustively dealt with in my Annual Report for 1908. Basing on the statements contained in the literature on the thymus gland and on the results of his investigations, the author comes to the conclusion that the thymus gland is an organ of growth, since there is a marked functional relationship between it and the development of the bones, the excitability of the nervous system, and the pupillary apparatus of the eye. There is a close relationship between the thymus gland and the other glands with internal secretion, especially between the thymus and the genital apparatus, while a number of anatomical and clinical manifestations point to the

Oser-Pribram, *Zeitschrift für experimentelle Pathologie* 1913, Vol. 12, p. 295.

* Compare Merck's Report 1911, p. 339.

Harrower, *Lancet* 1913, I, p. 524.

Basch, *Deutsche medizinische Wochenschrift* 1913, No. 30, p. 1456.

fact that the thymus is not only closely inter-related with the glands with an internal secretion, but also with the lymphatic apparatus of the body.

The therapeutic use of thymus gland is indicated, as is well known, *inter alia*, in the treatment of Graves's disease*. This is confirmed by Rahel Hirsch, who reports that she obtained good results by giving two thymin tablets daily. The authoress found that the preparation also has a soporific effect, which induced her to try it in insomnia in a number of patients. It displayed a good hypnotic action in diabetes insipidus, arterio-sclerosis, and in dyspeptic troubles.

Thyroid Gland. (Thyroidin.)

In epilepsy, the administration of thyroid gland is useful in those cases in which the thyroid gland fails properly to functionate; E. Gehna reports on two cases of this kind. The same may be said of thyroid medication in eclampsia gravidarum, according to E. L. W. Dunbar, when the thyroid is unable to fulfil the demands made of it during pregnancy. In two cases the author saw that the administration of thyroid gland caused the disappearance of the dizziness, albuminuria and œdema, and he therefore advocates energetic prophylactic treatment of eclampsia by means of this preparation.

M. Morris believes that a number of skin diseases of uncertain etiology are attributable to thyroid insufficiency, and for this reason he undertook exhaustive trials in various affections such as chronic psoriasis with myxœdematous manifestations, eczemas, sclerodermia, keloids, acanthosis nigricans, acne rosacea, lupus vulgaris and scrofuloderma. He gave to adults daily doses of 0.15 gramme ($2\frac{1}{2}$ grains), gradually increasing the dose to 0.6 gramme (10 grains); children were given 0.015 to 0.06 gramme ($\frac{1}{4}$ —1 grain). With this treatment he obtained very good results.

In the treatment of rheumatic affections of the joints, according to P. Claisse, the use of thyroid gland is effective only in selected cases, i. e., only in cases in which

* Compare Merck's Report 1908, p. 34.

Hirsch, Deutsche medizinische Wochenschrift 1913, No. 44, p. 2141.

Gehna, Revue de médecine 1913, No. 1.

Dunbar, British Medical Journal 1913, I, p. 1272.

Morris, British Medical Journal 1913, I, p. 1037.

Claisse, La Clinique 1913, No. 6.

there are dystrophic disturbances — disturbances of the functions of organs such as occur in cachexia strumipriva and in hypothyroidism. Of course, in severe changes of the joints such as ankylosis and destruction of the cartilaginous tissue, no cure can be expected from thyroid medication.

L. Thévenol and J. F. Percy have tried thyroid treatment in nephritis. Percy reports two cases which he treated with thyroid extract on the assumption that thyroid insufficiency was present. In one case he gave for one week four times daily 0.3 gramme (5 grains), and then for three weeks the same dose six times daily, with the result that the urine became normal, the blood pressure fell and the subjective troubles disappeared. In the other case he administered at first 2 grammes (30 grains), then 2.6 grammes (40 grains) daily and obtained a diminution of the nephritic and uræmic symptoms. Thévenol also considers thyroid medication useful in the treatment of nephritis, particularly in the forms associated with œdema. In agreement with other authors, in four cases he found that this therapy produced increased diuresis, subsidence of the œdema and a fall in blood pressure, but no increase in the albuminuria.

M. B. Gordon discusses the uses of, and indications for, thyroid therapy in children, e. g., in myxœdema, bodily and mental backwardness, enuresis, chronic rheumatoid arthritis and various skin diseases. D. M. Uspenski has published a review of the whole subject of thyroid therapy. Further, mention may be made of a paper by E. H. Waller who deals with the inter-relation of the thyroid gland and other internal secretions of sexual origin.

Ortizon.

Ortizon is a chemical combination of hydrogen peroxide and urea (carbamide) which contains 34 p. c. of H_2O_2 and

Thévenol, Progrès médical 1913, No. 19.

Percy, Journal of the American Medical Association, November 9, 1912.

Gordon, New York Medical Journal 1913, Vol. 97, p. 870.

Uspenski, Deutsche Ärzte - Zeitung 1913, No. 7—10.

Waller, Practitioner 89, 2; Deutsche Medizinal - Zeitung 1913, No. 11, p. 183.

is readily soluble in water. M. Strauss states that the preparation is issued in granular form, in sticks and in balls. The granular preparation is used for preparing an aqueous solution of hydrogen peroxide, etc., the balls are intended to provide a convenient means of preparing a mouth wash, while the sticks are used for the local treatment of wounds, fistulas and to arrest bleeding in hollow wounds, such as alveoles after extraction of teeth, radical operations on the middle ear, etc.

E. and F. Adler report on the use and value of ortizon balls in dental work. Each ball weighs 0.24 gramme (4 grains) and dissolved in water yields 0.1 gramme of hydrogen peroxide. For rinsing the mouth one ball is dissolved in half a glassful of lukewarm water, to which a little peppermint oil may be added to mask the taste of hydrogen peroxide. The aqueous solution of ortizon has been found useful in minor operations, ordinary stomatitis, inflammation of the palate, mercurial and ulcerative stomatitis. To cleanse putrid teeth powdered ortizon can be pressed into the teeth which have been mechanically cleansed and then moistened, whereby the decayed remnants are expelled by the gas which is liberated.

Engelhard also expresses a very favourable opinion of the value of ortizon in rhino-laryngological practice.

G. Blessing and F. Trümmer used ortizon sticks as a dressing for wounds. Trümmer used them as a caustic in epistaxis, rhagades at the nasal orifices, aphthous ulceration in the mouth and in perlèche. They stimulate granulation and have the advantage that the parts treated are not blackened, as is the case when using silver nitrate. Blessing never saw any injurious effects due to painful cauterisation, on the contrary, he believes that the carbamide present in the compound renders the procedure painless. He advises caution in introducing the stick into a wound since it may break if too much pressure is exerted.

Strauss, Allgemeine medizinische Zentral-Zeitung 1913, No. 8.

Adler, Deutsche zahnärztliche Wochenschrift 1913, No. 25.

Engelhard, Deutsche Medizinal-Zeitung 1913, No. 41.

Blessing, Deutsche zahnärztliche Wochenschrift 1913, No. 30.

Trümmer, Münchener medizinische Wochenschrift 1913, No. 46.

Ox Bile.

According to Drigalski and Bierast, Löffler's nutrient medium, which is eminently adapted for the diagnosis of diphtheria, may be rendered still more useful by the specific selective properties of ox bile, and under certain conditions possible sources of error in the examination may be excluded or lessened. The plates for cultural trials of diphtheria bacilli are prepared by mixing 600 c. c. of ox serum with 174 c. c. of glucose broth and 26 c. c. of bile. 16 c. c. of this mixture are placed into each of a number of Petri dishes which are placed in the serum coagulation apparatus until the mixture has set; they are then sterilized for three consecutive days. The plates are brushed in the ordinary manner and placed in an incubator at 37° C. According to the authors' statements the results obtained by this method are more reliable than those yielded by Löffler's method. F. C. R. Schulz has tested this method but he does not consider it to be more accurate, nor does the nutrient medium exhibit any improvement as regards its selective properties for diphtheria bacilli.

Pallidin.

O. Fischer and E. Klausner describe a new intra-cutaneous or cutaneous test for syphilis, which they have exhaustively investigated. It may be at once stated that this new test has the advantage over Noguchi's luetin* test of being specific for tertiary syphilis and for late heredo-syphilis, i. e., cases of paralysis and primary and secondary syphilis do not respond to this test. The reagent used is an extract prepared according to a special process from pieces of tissue from lungs affected with white pneumonia. I supply a reagent of this nature as a test for syphilis according to Fischer and Klausner under the name of "pallidin". The following technique is adopted:

The skin of the upper arm is lightly cleansed with ether. A sterile vaccination lancet is dipped into the extract and

Drigalski-Bierast, Deutsche medizinische Wochenschrift 1913, No. 26, p. 1237.

Schulz, ibidem 1913, No. 45, p. 2194.

Fischer-Klausner, Wiener klinische Wochenschrift 1913, No. 2, p. 49.

Klausner, ibidem 1913, No. 24, p. 973.

* Compare Merck's Report 1912, p. 400.

with it the skin is scarified in such a way that two pairs of parallel scarifications cross each other to form a square the sides of which are about 5 mm. long. Care should be taken to ensure as little bleeding as possible. The scarifications are allowed to dry; a protective dressing is unnecessary. In cases of tertiary and hereditary syphilis, and in isolated cases of late latent syphilis a typical reaction develops at the site of inoculation in the course of 36 to 48 hours. It consists in an intensely red papular efflorescence of 1 to 2 c. c. in diameter. In cases which respond by a very marked reaction small necrotic pustules appear along the course of the scarifications. The inoculation papules remain plainly visible for several days. With a negative reaction the scarifications can scarcely be distinguished after 48 hours, and the skin remains quite unchanged. A positive reaction never occurs in primary and secondary syphilis, nor in non-syphilitic individuals.

The mode of preparation of pallidin affords a guarantee for its harmlessness, since it is heated to 60° C. for a considerable period and 0.5 p. c. of carbolic acid is added to the reagent. In addition, it is tested by the authors before being issued, so that it may be employed without apprehension.

Papaverine.

Papaverine, which was discovered by G. Merck in 1848, belongs to those opium alkaloids which up to the present have not attained any special therapeutic importance. It was recommended by Leidesdorf as a hypnotic in mental cases, in doses of 0.03 to 0.06 gramme ($\frac{1}{2}$ —1 grain) by mouth, or 0.03 to 0.05 gramme ($\frac{1}{2}$ — $\frac{3}{4}$ grain) subcutaneously. However, after K. B. Hofmann, Funck, Frommüller, R. Elben and Bouchut had been unable to confirm the value of

Merck, Liebig's Annalen 1848, Vol. 66, p. 125 and 1850, Vol. 73, p. 50.

Leidesdorf, Wochenblatt der Wiener ärztlichen Gesellschaft 1868, Vol. 13, p. 115.

Hofmann, Wiener medizinische Wochenschrift 1868, p. 58. — Österreichisches medizinisches Jahrbuch, Vol. 20, p. 207.

Funck, Berliner klinische Wochenschrift 1869, No. 36.

Frommüller, Dissertation Erlangen 1869.

Elben, Dissertation Tübingen 1870.

Bouchut, Bulletin général de thérapeutique 1872, April.

papaverine, in spite of the brilliant results obtained by Baxt and the satisfactory effects reported by C. Stark, it was again forgotten* until Leubuscher tried it in children. In his experience it proved effective in diarrhoeas, especially in children. He gave to his patients, whose ages ranged from fifteen days to five years, doses ranging from 0.005 to 0.05 gramme ($\frac{1}{12}$ — $\frac{3}{4}$ grain).

According to the latest communications by J. Pal, G. Holzknecht and M. Sgalitzer, papaverine now appears destined to attain greater importance. For therapeutic purposes it is used in the form of pure crystalline papaverine and papaverine hydrochloride.

Papaverine, $C_{20}H_{21}NO_4$, occurs in white prisms which are soluble in alcohol, ether and chloroform. Melting point $147^{\circ}C$. It is almost insoluble in water.

Papaverine hydrochloride, $C_{20}H_{21}NO_4 \cdot HCl$, occurs in the form of colourless crystals, or as a white crystalline powder. It is readily soluble in water.

The therapeutic use of papaverine as proposed by Pal is based upon its action on smooth muscles in that it causes a condition of muscular relaxation, whereby the organs retain their individual movements, i. e., they are not paralysed. Also during the time that the action of papaverine is manifest the influence of the afferent nerves is merely lessened, but no paralysis of the nerves takes place. As far as the author was able to establish this reaction extends to the digestive tract, the gall-bladder, the bronchial musculature, the bladder, the uterus and the vessels. It manifests itself in the same way whether papaverine is applied locally or introduced directly

Baxt, Sitzungsberichte der Wiener Akademie der Wissenschaften 1868, Vol. 56, p. 189 and Archiv für Anatomie und Physiologie 1869 No. 1, p. 112.

Stark, Allgemeine Zeitschrift für Psychiatrie 1869, p. 121.

* Bernard's investigations showed that papaverine causes spasms, whereas Ott found that it acts at the same time as a convulsant and narcotic. (Bernard, Leçons sur les anesthésiques. Paris 1875. — Ott, British Medical Journal 1878, May.)

Leubuscher, Deutsche medizinische Wochenschrift 1892, p. 179. — Merck's Bericht 1892, p. 82.

Pal, Wiener medizinische Wochenschrift 1913, No. 17, p. 1049. — Medizinische Klinik 1913, No. 44, p. 1796.

Holzknecht-Sgalitzer, Münchener medizinische Wochenschrift 1913, No. 36, p. 1989.

into the blood stream. Pal emphasises the fact that papaverine influences all muscular elements of the same kind in an identical manner, which proves that it causes a muscular reaction in a wider sense. However, all tissues composed of smooth muscles do not react with equal sensitiveness. Thus E. Popper found in experiments on animals that the layer of longitudinal muscles of the surviving intestine of a rabbit reacted already to a solution of papaverine of 1:1,600,000, whereas the annular muscles reacted only to a 1:400,000 solution.

The intensity and duration of the action of papaverine show variations, whereby the tonicity of the muscle before the administration of papaverine plays a rôle. Its action is most marked when the smooth muscles are excited, i. e., when they are in a state of increased tonicity. In consequence of its action on smooth muscles papaverine acts as a depressant, and this effect may prove especially important in raised pressure; as a rule it depends upon the cause of the rise of pressure. For instance, it is extremely marked in the rise of pressure produced by adrenalin, and during the culminating period of the adrenalin effect it may cause a fall of pressure leading to a cessation of circulation or ventricular stillstand. This action on the vessels, discovered by Pal, induced the author to try cautiously the use of papaverine in man. In the experiments hitherto undertaken by him he administered papaverine hydrochloride in single doses not exceeding 0.08 gramme ($1\frac{1}{4}$ grain), and in daily doses not exceeding 0.24 gramme (4 grains). These amounts never produced any undesirable secondary effects; frequently diminution of action was observed but never any habituation to papaverine, as is the case with morphine. The author states that with the above mentioned doses the action on the vessels is insignificant, since they scarcely, if at all, influence normal blood pressure in man. Even in the presence of high blood pressure Pal failed to observe a depression such as occurs after amyl nitrite or chloral hydrate. Papaverine apparently only removes the excess pressure, a property which renders it especially valuable and assures it an important place among the depressants. Hence Pal obtained satisfactory results with papaverine in acute uræmia, cardiac asthma, angina pectoris and in the abdominal vascular crises in arterio-sclerosis and tabes. The action of papaverine is worthy of note in vomiting due to various

causes, such as vomiting in pregnancy, vomiting after chloroform anæsthesia and in sea-sickness, and also in gastric crises, in which the author records failures only in morphinism and in forms associated with hypersecretion. Further, Pal frequently succeeded in cutting short attacks of cholelithiasis by administering papaverine, and this treatment also exerted a favourable influence in dysmenorrhœa. Bronchial spasms and bronchial asthma offer further indications for papaverine, in which the drug usually displayed an efficient prophylactic and curative effect. In some cases the drug soon lost its action, but after stopping it for a short time small doses again proved effective. In these cases the dosage presents some difficulties, since there are cases which react promptly to a dose of 0.03 gramme ($\frac{1}{2}$ grain), whereas others require 0.06 gramme (1 grain).

Pal also draws attention to the fact that papaverine should prove useful in morphinism. Often the use of papaverine may obviate altogether the administration of morphine.

The antispasmodic effect of papaverine not only makes its therapeutic use appear justified, but, according to Pal, holds out great promise of its successful application for diagnostic purposes. Its use in this direction is particularly indicated in affections in the region of the intestines, since it makes it possible to distinguish spasm from purely anatomical disturbances. In cases where the spasm (pylorospasm) is the cause of pain, after twenty minutes papaverine displays a narcotic and analgesic effect, if it is given in sufficiently large doses; but if the pains are due to anatomical changes they are not relieved by papaverine. Further, since papaverine, in contradistinction to atropine, does not inhibit secretion, by the use of both alkaloids it is possible, under certain circumstances, to distinguish primary from secondary hyperacidity.

Papaverine plays an important part in the differential diagnosis of pylorospasm from pyloric stenosis, proposed by Holzkecht. He administered papaverine hydrochloride in doses of 0.05 to 0.07 gramme ($\frac{3}{4}$ — $1\frac{1}{12}$ grain) with Rieder's test meal, and by an X-ray examination noted the time taken for its evacuation. He found that with a healthy stomach evacuation is delayed by papaverine on an average to the extent of one-quarter to one-third of the time normally required. In addition, papaverine by reason of its antispasmodic effect abolishes the hypomotility due to pylorospasm.

Its effect of reducing the tonicity of the gastric musculature increases the hypomotility caused by the presence of pyloric stenosis; on the other hand, in the presence of both pyloric stenosis and pylorospasm the hypomotility remains constant.

According to Pal's latest communications papaverine possesses a further valuable property in that it displays an anæsthetising effect. The investigations undertaken by the author in collaboration with Finsterer show that papaverine produces anæsthesia of the mucous membranes and is an efficient local anæsthetic. Further, W. Zweig reports that a combination of papaverine and atropine proved useful in gastric ulcer. He injected daily 0.05 gramme ($\frac{3}{4}$ grain) of papaverine hydrochloride and 0.0005 gramme ($\frac{1}{125}$ grain) of atropine sulphate, and later increased the daily dose to double these amounts*.

Paracodin.

Dihydrocodeine, $C_{18}H_{23}NO_3$, obtained by Skita by the hydration of codeine, is issued under the name of "paracodin". It is a base melting at $65^{\circ}C$., which is soluble in alcohol and in water. Its tartrate and hydrochloride are still more soluble in water. Paracodin tartrate forms white crystals of the formula $C_{18}H_{23}NO_3 \cdot C_4H_6O_6, H_2O$, and paracodin hydrochloride occurs in white crystals having the composition $C_{18}H_{23}NO_3 \cdot HCl$.

The pharmacological investigation of paracodin by Gottlieb showed that paracodin displays a considerably greater sedative effect on the respiratory centre than codeine, i. e., 10 milligrammes of paracodin reduce the respiratory rate in a rabbit almost as much as do 25 milligrammes of codeine. Larger doses of both preparations cause accelerated respiration and an increase of the reflex excitability, whereby with paracodin a narcotic stage is manifest which is more marked than with codeine, which scarcely displays a narcotic action in rabbits. Hence the narcotic component is stronger

Pal, Finsterer, Zweig, *Münchener medizinische Wochenschrift* 1913, No. 49, p. 2736.

* Zweig has applied the name "Atropapaverine" to the solution of atropine and papaverine.

Skita, *Berichte der deutschen chemischen Gesellschaft Berlin* 1911, Vol. 44, p. 2865.

Gottlieb, communicated by Fraenkel.

in paracodin than in codeine. Otherwise the nature of its action points to its inclusion in the codeine group.

The results of its pharmacological investigation are borne out by A. Fraenkel's observations. He found that compared with codeine paracodin displays a quicker and more intense action as a remedy for coughs. The dose provisionally fixed by the author is 0.025 gramme ($\frac{2}{5}$ grain) of paracodin tartrate, three times daily. However, he believes that smaller doses may often suffice. On the other hand, he states that a dose of 0.05 gramme ($\frac{3}{4}$ grain) may be given without apprehension. Undesirable secondary effects occur just as rarely with paracodin as with codeine. G. Schwartz achieved equally satisfactory results; he gave paracodin in doses of 0.02 to 0.04 gramme ($\frac{1}{3}$ — $\frac{2}{3}$ grain) in advanced pulmonary tuberculosis. He says that the number of coughing attacks remained approximately the same as with the customary dosage of 0.04 gramme ($\frac{2}{3}$ grain) of codeine. Doses under 0.02 gramme ($\frac{1}{3}$ grain) frequently proved insufficient, whereas in most cases 0.03 gramme ($\frac{1}{2}$ grain) yielded the desired result.

W. Dahl tried paracodin in a large number of patients, especially to ascertain its tolerance on prolonged administration. As a rule, he gave in coughs, particularly in cough due to tracheitis, pleurisy and bronchitis, doses of 0.025 to 0.03 gramme ($\frac{2}{5}$ — $\frac{1}{2}$ grain), and he saw that the distressing cough was markedly relieved and sleep was improved. It also yielded good results in nervous insomnia. It exerted no influence on the expectoration, but it produced no habituation and never gave rise to any undesirable secondary effects, even on prolonged use.

Paraffin, Liquid

J. G. Chrysopathes states that the antiseptic and healing properties of liquid paraffin are apparently not so generally known as is desirable. At first he used it with surprisingly successful results in bedsores. The sores very soon became clean under the influence of liquid paraffin,

Fraenkel, Münchener medizinische Wochenschrift 1913, No. 10, p. 522.

Schwartz, ibidem 1913, No. 10, p. 525.

Dahl, Deutsche medizinische Wochenschrift 1913, No. 27, p. 1304.

Chrysopathes, Zentralblatt für Chirurgie 1913, No. 45, p. 1739.

whereby a fall in temperature was also observed. However, this preparation proved especially useful in the treatment of wounds, as the author had frequent opportunities of observing during the Balkan war. By its use he succeeded in effecting a remarkably speedy cure in over 600 wounded who came under treatment with suppurating wounds. Already after the first change of dressing even gaping wounds in which the bones were laid bare were cleansed to such an extent that healthy red granulations appeared. In very infected wounds the author used, in addition to pure liquid paraffin, a solution of 2 to 2.5 grammes of iodoform in 100 grammes of liquid paraffin with noteworthy results.

An explanation for this author's observations is afforded by the statements of Rost and Wacker. Rost ascribes the action of Beck's bismuth paste* to the American vaseline used in its preparation, or rather to the impurities contained in the latter. This is borne out by the successes reported by F. Esslinger, who found that in ulcers of the leg epithelization quickly followed the use of crude liquid paraffin. Moreover, Wacker and Schmincke have pointed out that certain crude liquid paraffins obtained from brown-coal tar possess in a marked degree the property of stimulating epithelization, whereas this is said not to be so marked with pure liquid paraffins.

Paraldehyde.

H. Noel and H. S. Souttar state that paraldehyde, when injected intravenously, displays a marked narcotic effect which sets in quickly and is comparatively deep. For this purpose they use a mixture of 5 to 15 c.c. of paraldehyde and the same amount of ether with 150 c. c. of a cold 1 p. c. solution of sodium carbonate; this is infused into a vein in the arm at the rate of 5 to 10 c.c. to the minute. The solution can be injected at ordinary temperature, or it may be warmed

Rost, compare this Report, p. 123.

Wacker, *Münchener medizinische Wochenschrift* 1913, No. 48, p. 2674.

* Compare Merck's Reports 1911 and 1912.

Esslinger, *Beiträge zur klinischen Chirurgie* 1913, Vol. 85, No. 3.

Wacker-Schmincke, *Münchener medizinische Wochenschrift* 1911, No. 30, p. 1607.

Noel-Souttar, *Annals of Surgery* 1913, Vol. 57, p. 64.

to 25° C. After about 40 seconds insensibility sets in which lasts for a more or less prolonged period, according to the amount of ether and paraldehyde employed. This method is said to have proved especially useful in alcoholics. However, it is applicable only to minor operations, and as a substitute for internal medication in conditions of excitement and in insomnia, when paraldehyde is refused owing to its nauseous taste.

O. Atkey was able to confirm the value of Noel's method in a severe case of tetanus. The case was that of a man, aged 19, who was given on several consecutive days intravenous injections of at first 5 c.c. of paraldehyde and 5 c.c. of ether, then on the following days 15 c.c. of paraldehyde and ether, and once as much as 30 c.c. In addition, large amounts of physiological salt solution were infused. At first this treatment displayed only a transient action, gradually, however, improvement set in and after sixteen days all the tetanic manifestations had disappeared. The author believes that the injections of paraldehyde exerted a beneficial influence on the nervous exhaustion and relieved the pains, so that in spite of the spasms the patient's condition of nutrition remained good. Even larger doses of paraldehyde may be used.

G. Heyl describes an interesting test for purity of paraldehyde, which is based upon the estimation of the amount of acetaldehyde present in paraldehyde. To carry out this test 25 grammes of paraldehyde are added to 300 c.c. of well cooled water in a wide-necked flask, with agitation, whereupon 30 c.c. of normal solution of potassium hydroxide and 20 c.c. of perhydrol are added. After carefully mixing the whole is allowed to stand overnight (well closed), and is then titrated with normal solution of hydrochloric acid, using phenolphthalein as indicator. By this method the acetaldehyde present is oxidised by the perhydrol* to acetic acid, which is neutralized by the potassium hydroxide. Therefore, when titrating back with hydrochloric acid less normal solution of hydrochloric acid will be required than was added of normal solution of potassium hydroxide. The amount of solution of

Atkey, *Lancet* 1913, I, p. 168.

Heyl, *Apotheker-Zeitung* 1913, No. 73, p. 720.

* Compare Lunge-Berl, *Chemisch-technische Untersuchungsmethoden* 1911, Vol. 3, p. 922.

potassium hydroxide neutralized by the acetic acid multiplied by 4×0.04403 indicates the percentage of acetaldehyde present in the paraldehyde under examination. If this test shows that less than 3.15 p.c. of acetaldehyde is present, another test should be undertaken using a larger amount of paraldehyde in corresponding dilution. Further, the acidity of the paraldehyde should be estimated and this factor also taken into account.

Para-Monochlorphenol.

Para-monochlorphenol now occupies a recognized position* as an antiseptic in dental work, and during the past year Möller again drew attention to its extremely valuable properties. However, since Triebel and Kurkiewicz deprecated the use of chlorphenol on account of its caustic action and advocated its substitution by chloral hydrate, G. Blessing again speaks in favour of chlorphenol and shows that its use is fully justified. Compared with chloral hydrate it has the advantage of being a very much more powerful disinfectant, and, as is the case with phenol**, camphor is added to mitigate its caustic effect. However, if any injury to the tissues is apprehended from the application of chlorphenol-camphor (1:2), Blessing states that a dilution of this preparation may be used. Alcohol cannot be used for this purpose on account of its irritant action upon wounds; on the other hand, acetone is very suitable for this purpose, especially if a little water is added. The author gives the following prescription:

Rp. Para-monochlorphenol.	1 gramme (15 grains)
Camphor.	1 „ (15 „)
Acetone	6 grammes (125 min.)
Aq. dest.	3 „ (50 „)

Although in this solution the chlorphenol-camphor is diluted $5\frac{1}{2}$ times, its disinfectant action, according to Blessing, is

* Compare Merck's Reports 1896, p. 125; 1902, p. 137 and 1910, p. 276.

Möller, *Odontologische Nachrichten* 1912, No. 23.

Triebel, *Zahnärztliche Rundschau* 1911, No. 23.

Kurkiewicz, *ibid.* 1911, No. 28.

Blessing, *Deutsche Monatsschrift für Zahnheilkunde* 1913, No. 8, p. 650. Compare Merck's Report 1910, p. 276.

** Compare the article on Phenol-Camphor in this Report.

still sufficiently powerful to ensure a reliable result. In the author's experience chlorphenol-camphor, used per se or in the above dilution, will maintain its position as a valuable remedy, and whoever has once tried it will be loth to give it up. The author cannot recollect having met with an unpleasant experience due to the drug, although he has used it in several hundreds of cases.

L. de Renier reports that he has obtained favourable results with monochlorphenol in the treatment of lupus and pharyngeal tuberculosis. His method consists in rendering the affected part insensible by the application of a 10 p. c. solution of cocaine, whereupon the preparation is applied to the mucous membranes; this treatment is repeated every second or third day.

Perhydrit.

As I already stated in last year's Report, perhydrit is a solid form of hydrogen peroxide which, like the liquid preparation, possesses all the advantages of an ideal dressing for wounds. It can be used not only in aqueous solution in the same way as an ordinary solution of hydrogen peroxide, but also in solid form, in the shape of sticks, for the treatment of wounds, bleeding, and fistulas. Since it contains 34 to 35 p. c. of H_2O_2 , to prepare a 1 p. c. (or 3 vol.) solution of hydrogen peroxide 3 grammes are dissolved in 100 grammes of water (or 60 grains in 4 oz), a solution of 6 grammes in 100 grammes of water yields a 2 p. c. solution, and 9 grammes dissolved in 100 grammes of water a 3 p. c. solution, and so forth. According to J. Schumacher, to facilitate calculation the number 33.3 should be borne in mind. Thus, by dissolving 1 gramme of perhydrit in 33.3 grammes of water a 1 p. c. solution of hydrogen peroxide is obtained, by dissolving 2 grammes in 33.3 grammes of water a 2 p. c. solution, and so forth. Schumacher's investigations show that a solution of this kind exhibits the same properties as an ordinary solution of hydrogen peroxide. In a freshly prepared solution of perhydrit catalysts (metallic silver, manganese peroxide, etc.) cause the libera-

Renier, Westnik po Terapii Tuberkulesa 1913, Vol. 2, p. 2.

Schumacher, Deutsche medizinische Wochenschrift 1913, No. 46, p. 2253.

tion of oxygen under frothing. Also in substance the preparation is decomposed by catalysts with liberation of oxygen. This proves that the hydrogen peroxide is present in perhydrit in a loose combination and that the liberation of oxygen takes place with sufficient rapidity for therapeutic purposes. The other chemical properties, such as oxidising and reducing action, are displayed by perhydrit in the same way as with perhydrol. For this reason the clinical uses and indications are the same for perhydrit as for perhydrol. Thus in a case of double-sided inguinal buboes the author caused the disappearance of the foul odour of the wound secretion within a few days by daily irrigations with a 1 p.c. solution of perhydrit. He obtained the same success in other cases of hard ulcers. Further, in mercurial treatment he succeeded in preventing the occurrence of stomatitis by prescribing a 2 p.c. solution of perhydrit as a mouth wash.

F. Watry also employed perhydrit with excellent results in all cases in which the use of a solution of hydrogen peroxide was indicated. Perhydrit tablets are convenient and easy to carry, and permit the preparation of a comparatively large amount of solution of hydrogen peroxide. Watry used perhydrit, *inter alia*, in a case of black hairy tongue, in which ordinary solution of hydrogen peroxide had proved ineffective, probably on account of its rapid deterioration.

The bactericidal action of perhydrit is confirmed by E. Ungermann. He states that perhydrit is a preparation which embodies the bactericidal properties of hydrogen peroxide in a hitherto unsurpassed concentration and in a highly active, and still sufficiently stable form. A 3 p.c. solution is capable of destroying within fifteen minutes, at ordinary temperature, the most resistant bacteria and spores, and this action is considerably increased at a higher temperature. On the mucous membranes and in the mouth this action is exhibited in such a degree that perhydrit is assured of a favoured place among the commercial preparations of hydrogen peroxide. From a paper by A. Marcuse it is apparent that the chemical properties and reactions of perhydrit are identical with those of hydrogen peroxide.

Watry, *Anvers médical* 1913, No. 4.

Ungermann, *Hygienische Rundschau* 1913, p. 1137.

Marcuse, *Pharmazeutische Zeitung* 1913, No. 94.

Perhydrol.

J. Wolpe has undertaken a series of experiments to elucidate the action of hydrogen peroxide in gastric and intestinal affections. In cases of hyperacidity, hypersecretion, gastric ulcers and dilatation of the stomach he adopted Petri's method, or a modification of the latter in that he did not administer the solution of hydrogen peroxide with the test meal, but gave it after the patient had eaten a roll and drunk half a glassful of water. After 45 minutes the patient was given either 200 to 250 c.c. of 0.5 p.c. solution of hydrogen peroxide, or one teaspoonful of magnesium-perhydrol in half a glassful of water. Basing on his observations the author came to the following conclusions: Solution of hydrogen peroxide diminishes the acidity of the gastric juice, especially the free hydrochloric acid; it increases the secretion of mucus and thereby neutralises the acid gastric juice; an increase of the secretion of gastric juice does not take place. — In fermentative processes in the stomach (dilatation of the stomach, stenosis and pylorospasm, carcinoma of the stomach, incomplete achylia gastrica, etc.) hydrogen peroxide acts as an antiseptic. — In hyperacidity, hypersecretion and *ulcus ventriculi* it is very useful as a antacid. — On the other hand, its use is contraindicated in well defined gastritis with secretion of mucus, as in these cases a secretion of mucus is not desired, and in complete achylia gastrica and in gastric ulcers with profuse bleeding during the periods of increased gastric peristalsis. — Hydrogen peroxide considerably reduces intestinal fermentation, as well as acid carbon dioxide and nitrogenous fermentation, it paralyses the action of intestinal bacteria and of the excitors of fermentation. Its inhibitory effect on fermentation is manifest in the disappearance in the urine of indican and ethyl sulphuric acids. — In chronic colitis and intestinal ulcers hydrogen peroxide diminishes the local irritation; this effect is due to its disinfectant action and the decrease in the amount of gas.

On account of its disinfectant action perhydrol is a useful prophylactic against post-operative peritonitis in the treatment

Wolpe, *Wratschebnaja Gazeta* 1913, No. 18, p. 653 and No. 19, p. 679. — Compare M. Henius, *Medikamente in der Therapie des Ulcus ventriculi chronicum und seiner Folgezustände*. *Zeitschrift für Chemotherapie und verwandte Gebiete*, Vol. II. (Ref.), p. 730.

of soiled laparotomies. O. von Herff's experiments show that perhydrol will in future compete with camphorated oil which has recently been largely used for the same purpose, but which has not always proved uniformly successful. The author used perhydrol exclusively in profuse and sanious suppuration, and regularly after abdominal hysterectomy for carcinoma of the uterus. In the former cases undiluted perhydrol was applied without any injury, and later a dilution of one part with two parts of distilled water. Von Herff gives the following illustration of the use of perhydrol: "Abdominal hysterectomy. After removal of the uterus and cleansing of the pelvis under drainage into the vagina the margins of the peritoneal wound are clamped and about 20 to 30 c. c. of perhydrol are poured into the pelvic wound. This is immediately followed by considerable frothing which covers everything. After a few minutes so much of the froth is removed to enable the margins of the wound to be seen. During this procedure warmth is produced which according to my observations ranges between 35° and 45° C. The whole of the wound area is carefully covered by the peritoneum, and about 10 c. c. of perhydrol solution are again poured in; the peritoneum is sutured and perhydrol is again applied to the sutures of the muscles and fascia; the skin is closed." Von Herff states that with this treatment there is a risk of perhydrol causing intestinal adhesions. The author is unable to express a positive opinion on this point as his experiments are not yet concluded; however, he states that in one case, which he describes in detail, no intestinal adhesions were observed. As perhydrol is non-toxic von Herff advocates a further trial of his method.

Perhydrol has also proved an excellent bactericide in the treatment of laryngeal and pharyngeal diphtheria, angina follicularis, lacunaris and catarrhalis, even in severe cases in which the patients on account of their age and want of intelligence were incapable of effecting by themselves a disinfection of the affected parts of the throat by gargling, so that treatment had to be carried out by a third person. According to Köhler the treatment consists in painting hourly with a 10 p. c. mixture of perhydrol and glycerin; in adults this is

Von Herff, *Gynäkologische Rundschau* 1913, Vol. 7, No. 1.

Köhler, *Klinisch-therapeutische Wochenschrift* 1913, No. 3, p. 81.

supplemented by gargling with a 2 p. c. solution of perhydrol. The injection of diphtheria antitoxin and other useful measures should not be neglected. The perhydrol-glycerin mixture not only disinfects but produces an abundant froth which carries away the mucus and diphtheritic membranes. Hence in these cases the perhydrol displays a bactericidal effect and also acts as a mechanical detergent.

For irrigations in pyelitis, to cleanse the renal pelvis, indifferent fluids such as sterile water, physiological salt solution, etc., are used, as well as antiseptic solutions, such as solutions of boric acid, collargol, or silver nitrate. J. Hartmann considers perhydrol to be the best agent. He used it at first in 1 to 2 p. c. solution, and later in 0.25 to 0.5 p. c. solution, as he was able to demonstrate by means of control plates that it displays an excellent bactericidal action and does not cause any irritation. The use of very concentrated solutions alone causes secondary effects such as pains, which are probably due to tension of the renal pelvis in consequence of the liberation of too great an amount of oxygen. However, the use of very dilute solutions is quite effective, since their antiseptic action is sufficient.

Douglas Freshwater recommends the use of perhydrol as a mild depilatory. For this purpose he uses the following ointment, which is very convenient in use:

Rp. Perhydrol	9 grammes (3ijss)
Adip. Lanae anhyd.	23 grammes (3vj)

Papers of otological interest have been published by H. Klau and G. Brühl. Klau discusses the treatment of chronic middle-ear suppuration, and he draws attention to the fact that in cases in which it is not possible to remove the secretion by syringing from the external auditory canal, it is necessary to irrigate the tympanic cavity from the tube. According to Klau, if a few drops of a 3 p. c. solution of perhydrol are subsequently instilled into the ear, after careful drying, this materially assists the action of the irrigations. The ear should again be dried after the instillation. In the place of irrigations Brühl has employed for years in acute and chronic middle-ear

Hartmann, *Praktische Ergebnisse der Geburtshilfe und Gynäkologie* 1913, Vol. 2, I, p. 162.

Freshwater, *Practitioner* 1913, May.

Klau, *Allgemeine medizinische Zentral-Zeitung* 1913, No. 22, p. 261.

Brühl, *Ärztliche Sammelblätter* 1913, No. 20.

suppuration a mixture of 60 grammes (2 oz) of solution of hydrogen peroxide and 100 grammes ($3\frac{1}{2}$ oz) of water, or a mixture of 6 grammes (100 min.) of perhydrol and 94 grammes ($3\frac{1}{3}$ oz) of water*. After wiping the auditory canal with cotton wool the patient's head is inclined in such a way that the ear is directed upwards, the auditory canal is stretched by pulling the auricle backwards and upwards and the solution of perhydrol is poured out of the bottle directly into the auditory canal, in which it is allowed to remain for one to three minutes. It is then allowed to run out and the ear is carefully dried with cotton wool. In the presence of abundant suppuration this treatment may be repeated several times in succession. It disinfects, deodorises and cleanses the ear and prevents the pus from stagnating or from penetrating deeper, and does not produce any unwelcome secondary effects. However, the use of perhydrol does not do away with the need for local treatment.

In regard to the use of perhydrol in dental work reference may be made to some communications by G. Mahé and P. Vanel, A. Sigrist, J. Steinkamm, H. Hille, Jesenski and Wachsmann, H. Levy, N. Black and A. Morgan.

Mahé and Vanel describe a method of inducing anæsthesia in which a combination of perhydrol and cocaine is used in the place of adrenalin, since the latter may inhibit the regeneration of tissue and cause inflammation at the site of injection. They inject 4 c. c. of a 0.5 p. c. solution of cocaine hydrochloride to which one drop of perhydrol is added. The injection is best made with a platinum or nickel needle and the amount is divided into three portions, i. e., an injection is made into both sides of the tooth and a third injection

* 60 grammes of official solution of hydrogen peroxide and 100 grammes of water yield a 1.12 p. c. solution of H_2O_2 ; 6 grammes of perhydrol and 94 grammes of water yield a 2 p. c. solution of hydrogen peroxide. The latter is preferable since perhydrol is free from acid and therefore does not cause irritation.

Mahé-Vanel, *Presse médicale* 1913, No. 33, p. 329.

Sigrist, *Zahnärztliche Rundschau* 1913, No. 8.

Steinkamm, *Deutsche Zahnärztliche Wochenschrift* 1913, No. 23.

Hille, *ibidem* 1913, No. 18.

Jesenski-Wachsmann, *Zubni Lékarstwi* 1913, No. 5, p. 109.

Levy, *Deutsche Zahnärztliche Wochenschrift* 1913, No. 24.

Black, *Dental Record* 1913, Vol. 33, No. 5, p. 285.

Morgan, *ibidem* 1913, Vol. 33, No. 5, p. 299.

externally into the surface of the palatine bone in the direction of the root. It is essential not to make the injections into the deeper layers of the mucous membranes, because if the injection is made between the mucous membrane and the periosteum the amount of anæsthesia produced is unsatisfactory. To prevent pain the injection must be made slowly. By this means a smaller amount of the injection fluid is required and the anæsthesia passes off in a shorter time. With this method cocaine is apparently superior to novocaine. The operation (extraction) usually takes place without loss of blood or there is very slight bleeding which is quickly arrested.

Perhydrol is a very useful agent for bleaching teeth, as I have already stated in these Reports*, especially in combination with light treatment. Its use in this direction is discussed by the other above cited authors. Sigrist studied the action of solutions of perhydrol and of perhydrol mouth wash on various fillings and gold work in the mouth, and after many years' experience of both preparations he has been unable to observe any injurious effect.

A communication by Sieber-Schumowa on the hydrolysing power of hydrogen peroxide is worthy of note, as the latter may prove useful in combating tuberculosis. The author was able to demonstrate experimentally that a 1.5 p. c. solution of hydrogen peroxide completely dissolves tubercle bacilli within ten minutes. Further, experiments on animals showed that tuberculosis could not be produced by the introduction of tubercle bacilli which had been submitted to a preliminary treatment with solution of hydrogen peroxide.

J. Frucht, Fouet and Scheidt report on the use of perhydrol in veterinary surgery. Frucht treated a fistula of the withers in a horse by injections of a 1 p. c. solution of hydrogen peroxide with the result that the suppuration diminished day by day, granulations rapidly formed and the wound closed on the thirteenth day of treatment. The wound was then twice dusted with tannoform. The horse, which

* Compare Merck's Report 1911, p. 346.

Sieber-Schumowa, Petersburger medizinische Wochenschrift 1913, No. 7, p. 84.

Frucht, Österreichische Wochenschrift für Tierheilkunde 1913, No. 42, p. 510.

Fouet, Berliner tierärztliche Wochenschrift 1913, No. 15, p. 277.
Scheidt, Münchener tierärztliche Wochenschrift 1913, No. 27, p. 513.

had been given over to the knacker as incurable, was discharged two days later cured and was able to resume work.

Fouet records the results obtained by the use of solution of hydrogen peroxide in tetanus in horses. After disinfecting the site of injection the author injected morning and evening 60 to 150 c. c. (2—5 oz) subcutaneously, or 100 to 160 c. c. ($3\frac{1}{2}$ — $5\frac{2}{3}$ oz) intravenously into the jugular vein. In the latter case he first injected a small amount of boiled water or of physiological salt solution to prevent blocking of the needle. Four of the horses treated by this method recovered, two died.

For a severe wound in a horse Scheid prescribed a 3 p. c. solution of hydrogen peroxide as well as the use of a dusting powder consisting of a mixture of exsiccated alum, boric acid and wood charcoal, and by this means effected a cure within sixteen days. The author states that he has found perhydrol an excellent dressing for wounds.

W. Eichholz's investigations show that a 3 p. c. solution of hydrogen peroxide is well adapted for disinfecting utensils made of metal, such as surgical instruments, and dishes made of iron, nickel or copper (but not silver). However, it is essential that the preparation used be chemically pure. Iron is not attacked by pure hydrogen peroxide in 30 p. c. concentration nor by weaker solutions. This fact may even be utilised to establish the purity of a preparation of hydrogen peroxide. However, in applying this "iron test" care must be taken to exclude possible impurities in the reagents used (in the distilled water), and in the glass apparatus (Jena glass). Compared with all other preparations of hydrogen peroxide perhydrol, owing to its purity, attacks iron the least. In the case of combinations of hydrogen peroxide and urea (perhydrit) the action on copper is more characteristic of their purity than the action on iron.

For practical purposes disinfection with pure hydrogen peroxide (solutions containing 3 p. c. of hydrogen peroxide prepared from perhydrol or perhydrit) is indicated in cases where sterilisation by boiling is not practicable for any reason, this is especially the case with dental and veterinary instruments. Ordinary commercial solutions of hydrogen peroxide cannot be used for this purpose.

Phenol-Camphor (*Camphora Phenylica*).

Phenol-camphor, according to V. Chlumsky's directions, is prepared by mixing 30 parts of phenol, 60 parts of camphor and 10 parts of alcohol, and was recommended by this author as an excellent, non-caustic remedy for the treatment of erysipelas. Its good action has been confirmed by a number of observers*. Recently Chlumsky has again drawn attention to phenol-camphor and reports his experience with this preparation since his first publication. He states that this preparation has proved a specific in erysipelas, and he says that no other remedy displays so prompt or reliable an action. Moreover, its application is extremely simple. The affected parts and their immediate vicinity are painted with the preparation, and where an extensive area is affected compresses impregnated with the solution are applied. In the majority of cases the temperature is said to return to normal already after twenty-four hours and the morbid process is arrested. It is not advisable to cover the cotton wool with Billroth's cambric, since this occasionally causes the phenol-camphor to display a slightly caustic action. According to the severity of the affection the dressing is changed once to three times daily. In most cases, especially in recent cases, a complete cure is effected in from two to three days.

Chlumsky has found that phenol-camphor is also effective in several other affections which are possibly due to streptococcal infection. Thus in severe rheumatic affections of the joints and muscles** accompanied by high fever and which did not react to salicylates, he applied compresses impregnated with phenol-camphor and saw a very beneficial influence on the manifestations. The same treatment is also very effective in infected wounds, furuncles, whitlows, mastitis and phlegmons, in which the preparation can be poured

Chlumsky, Zentralblatt für Chirurgie 1905, No. 33. Merck's Report 1905, p. 45.

* Compare Merck's Reports 1906, p. 190 and 1907, p. 192.

Chlumsky, Klinisch-therapeutische Wochenschrift 1913, No. 22, p. 653.

Chlumsky, Zentralblatt für innere Medizin 1912, p. 226.

** Phenol-camphor is also placed on the market under the name of "kamphenol" and "erysol". (Compare Klinisch-therapeutische Wochenschrift 1913, p. 655.)

directly into the wound. The discharge quickly diminishes, the wounds become clean and heal; however, in order to prevent the formation of cysts care must be taken not to allow the wounds to close too quickly; they must remain open until the discharge has ceased entirely.

In tuberculous fistulas in which a secondary infection with other micro-organisms was also present phenol-camphor was used with successful results, but it failed to influence sufficiently the primary affection.

K. Rühl discusses the value of phenol-camphor in syphilitic sores, in which the preparation was first used successfully by Franceschini. He adopted the modification proposed by Piccardi and published in his handbook. The sore is wiped with a pledget of cotton wool impregnated with a solution of mercuric chloride 0.5—1:1000, the wound is repeatedly touched with phenol-camphor and dusted with an antiseptic powder and suitably dressed with cotton wool. On the two following days the treatment with solution of mercuric chloride and the dusting with the antiseptic powder is carried out by the patient himself two or three times daily, whereupon the above described procedure is again performed by the medical attendant. In abnormally malignant sores a pledget of cotton wool impregnated with phenol-camphor is applied to the wound and is removed by the patient after twenty-four hours, whereupon for one day he himself carries out the treatment with the solution of mercuric chloride and the dusting powder. It depends upon the condition of the sore whether the application of phenol-camphor, as described above, is continued either by touching with the preparation, or by applying it as a compress. A waterproof dressing is not applied.

With this treatment the author always obtained highly satisfactory results. Healing took place at least as quickly, and in several cases sooner than with other methods. In addition, the application of phenol-camphor is painless in comparison with other preparations which cause pain, such as zinc chloride, silver nitrate and iodine.

Rühl, Deutsche medizinische Wochenschrift 1913, No. 34, p. 1643.
Franceschini, Giornale italiano delle malattie veneree e della pelle 1906, p. 635.

Piccardi, La terapia medica, chirurgica e fisica nelle malattie cutanee e veneree. Turin 1912.

Rühl also prescribed phenol-camphor in several cases of suppurating lymphatic glands (buboes). After incision of the abscess he poured in a few drops, or plugged or drained the wound with strips of gauze which had been dipped in phenol-camphor.

The mode of action of phenol-camphor still awaits explanation. The phenol is unquestionably the principal factor, however, the camphor doubtless possesses a considerable antiseptic power. Nevertheless, it is a remarkable fact that in spite of the large amount of phenol present in the mixture with camphor it should have entirely lost its irritant action, so that undiluted phenol-camphor can be applied without apprehension to wounds and fistulas. F. Horowitz demonstrated that not the camphor but the alcohol abolished the irritant action of phenol; his investigations show that alcohol is a valuable antidote to carbolic acid and might prove very useful in cases of internal poisoning by phenol. In such cases he introduces alcohol in any form, such as spirit of wine, brandy, etc., by means of a tube into the stomach, which is emptied after a few minutes to avoid acute alcoholic poisoning. In his experience it is sufficient if the alcohol comes into contact with the phenol.

Phenolphthalein.

As is well known, phenolphthalein* is extensively used as a laxative. In spite of its extensive use, when taken in appropriate doses, undesirable secondary effects have been very rarely observed, and in the few cases in which these have occurred they were doubtless due to a special individual susceptibility. The preparation is quite free from toxic properties, and this is confirmed by F. Orland, who reports the case of a child, aged 3 years, which while unobserved took 1·8 grammes (27 grains) in the form of purgen tablets (18 tablets). The only effect was that the child shortly afterwards complained of abdominal pain, followed by diarrhoea which lasted for about two days. On the first day the

Horowitz, Deutsche medizinische Wochenschrift 1913, No. 39, p. 1886. — Compare also: L. Berceller, *ibidem* 1913, No. 48, p. 2353.

* Compare Merck's Reports 1903—1908.

Orland, Medizinische Klinik 1913, No. 7, p. 257.

stools had a grey to greyish-green colour, on the second day they were grass-green, then again formed and of normal colour. The addition of solution of potassium hydroxide to the faeces produced an intense red colour, and for four days the urine gave the phenolphthalein test, but contained neither albumin nor sugar. A striking decrease in the amount of urine passed during the first two days took place, during which only 100 c. c. of urine were passed per diem, but no disturbances referable to the urinary organs occurred. However, in view of the large amount taken it is an open question whether every case would run so favourable a course. J. Erdős reports the case of a child, aged 5, which had taken by mistake 8 purgen tablets. After an hour excitement and disturbance of consciousness occurred, in addition to redness and puffiness of the face, quickening pulse, nausea and pains in the stomach. These symptoms yielded only after vomiting. This case shows that phenolphthalein cannot be regarded as harmless; on the other hand, it is not poisonous, as is apparent from the first case. However, both instances show very forcibly the necessity of putting medicines of this kind out of the way of children, since similar experiences may easily occur with other remedies which are on the whole innocuous, such as santonin tablets, rhubarb pills, etc.

To detect phenolphthalein in urine, especially when the urine has a dark colour, Bardach states that the spectro-scope may be used. He found that an alkaline urine, or a urine rendered alkaline, containing phenolphthalein, such as may occur after taking purgen, shows an absorption-band between D and E. It may be mentioned that Flatow and Brünell use a solution of phenolphthalein 1:50 000, rendered alkaline by the addition of a little soda, as a standard solution in the colorimetric estimation of urobilin in urine. For details of the method the original paper should be consulted.

Phenolsulphonephthalein.

Further reports* regarding the use of phenolsulphonephthalein for testing the renal function have been published

Erdős, Orvosi Hetilap 1913, p. 124.

Bardach, Wiener klinische Wochenschrift 1913, No. 4, p. 141.

Flatow, Münchener medizinische Wochenschrift 1913, No. 5, p. 234.

* Compare Merck's Reports 1911 and 1912.

by H. K. Bonn, Albrecht, M. Roth, E. Eichmann, F. S. Sondan and Th. W. Harvey, F. Erne, F. Fromme and C. Rubner, E. Behrenroth and L. Frank, G. Goodman, Fishbein and Dietsch.

The method already described in my Reports is said by Goodman to have proved very useful in a variety of cases of general as well as organic diseases. Dietsch came to the same conclusion. If, on the one hand, phenolsulphonaphthalein possesses the property of disturbing or harming the renal function, and, on the other hand, it is eliminated within a short time and under normal circumstances in a certain ratio and in a fixed percentage, this shows, according to Dietsch, that it is a dye which is eminently adapted for testing the renal function. This test furnishes information of great value regarding the functional ability of the kidneys. Both authors agree that in unilateral kidney disease the same result can be obtained by ureteral catheterization. Further, in the presence of both cardiac and renal decompensation this test makes it possible to ascertain whether a primary cardiac or renal affection is the cause of the disease, without resorting to the use of cardiac tonics or other methods involving a loss of time. In addition, this test serves to demonstrate renal insufficiency in cases in which the clinical examination of the patient gave no evidence. Behrenroth and Frank state that there is a certain parallel between the degree of functional derangement and the elimination of the dye. The authors also found that in chronic interstitial nephritis the time of appearance as well as the total elimination of the dye are delayed, whereas

Bonn, Journal of the Indiana State Medical Society 1913, Vol. 6, p. 154.

Albrecht, Zentralblatt für Gynäkologie 1913, No. 9, p. 316.

Roth, Berliner klinische Wochenschrift 1913, No. 35, p. 1609.

Eichmann, Zentralblatt für Gynäkologie 1913, No. 6, p. 198.

Sondan-Harvey, Deutsche medizinische Wochenschrift 1913, No. 10, p. 478.

Erne, Münchener medizinische Wochenschrift 1913, No. 10, p. 510.

Fromme-Rubner, *ibid.* 1913, No. 11, p. 588.

Behrenroth-Frank, Zeitschrift für experimentelle Pathologie 1913, Vol. 13, p. 72.

Goodman, Journal of the American Medical Association 1913, Vol. 61, p. 184.

Fishbein, Medical Chronicle 1913, Vol. 58, p. 239.

Dietsch, Zeitschrift für experimentelle Pathologie 1913, Vol. 14, p. 512.

in oliguria with chronic cardiac insufficiency the excretion of phenolsulphonephthalein is not influenced.

The value of the phenolsulphonephthalein test has been favourably criticized by Erne, Bonn, Sondan, Fishbein and Harvey. Albrecht, on the other hand, maintains that it cannot displace Albarran's functional test, however simple and tempting it may seem. In any case a number of precautions must be observed while applying the test, and these are fully discussed by Roth. The author, *inter alia*, points out that the test should not be made in women with diseases of the genitals and during pregnancy. He also says that the injections should be made intramuscularly, in accordance with the instructions of the originator of the test, into the lumbar muscles, since intragluteal injections often yield false, sub-normal values. Fromme and Rubner also mention that intramuscular injections yield unreliable results, and they advocate intravenous exhibition. With normal kidneys 60 to 65 p. c. of the phenolsulphonephthalein injected (intravenously) should be eliminated within the first three hours; as a rule, a larger amount is excreted, and up to 90 p. c. may be recovered. Eichmann came to similar conclusions; phenolsulphonephthalein should be injected intravenously; for with intramuscular injection it is by no means a matter of indifference whether the dye is injected directly into a muscle or into an interspace. Further, with intravenous injection the preliminary conditions are likely to be the same in every case, whereas with intramuscular injection the filter to be passed (muscle) may differ in every case. Uncomplicated cystitis and pyelitis can be distinguished from nephritis by this test. Obstruction due to cardiac insufficiency also appears to delay the elimination of the dye. However, he warns against forming too optimistic an opinion of the value of the test, for although it is extremely useful, together with the customary methods of examination, it would be premature to base the diagnosis or prognosis upon it alone, and in the author's opinion further experience is necessary.

Phenyldimethyl-Pyrazolone (Antipyrine).

L. W. Reynolds' paper is an interesting contribution to the treatment of obstinate sciatica. He reports the

case of a man, aged 66, suffering from sciatica who had derived only slight benefit from various forms of treatment such as baths, massage, electricity, etc. His condition became worse after the last treatment, and could not be influenced by electric light baths, cantharides plaster, potassium iodide or salicylates. The patient was able to lie only on his left side, since the pain involved the whole of the right side from the hip downwards. The author decided to try injections of phenazone*, and for this purpose used a solution of 10 grammes of phenazone and 0.15 gramme of cocaine hydrochloride in 10 c. c. of water; 1 c. c. being injected into the upper part of the thigh over the nerve. The injections were repeated every two days, at different places along the course of the nerve, an interval of three or four days being allowed after every third dose. Nine injections were given in all. No pain was caused at the time, but after six hours severe pain was experienced which occasionally necessitated an injection of morphine. For three weeks this treatment yielded no marked improvement, but apparently greater relief from the pains was experienced the nearer the fluid was injected to the nerve-trunk. Thus, marked relief was obtained when the injection was made over the external popliteal behind the head of the fibula, and when it was made on the dorsum of the foot the pain was completely removed after four hours. The patient's condition rapidly improved from the day on which the injection was made in the vicinity of the popliteal space. However, slight cardiac disturbance occurred as well as slowing and intermittent pulse, which was quickly controlled by strychnine and digitalis. The improvement was maintained and the patient was able to walk, although the leg still remained stiff.

Phobrol.

According to K. Zahn, phobrol is a 50 p. c. solution of chloro-meta-cresol** in potassium ricinoleate. It is a clear, brown liquid, which on mixing with water yields an almost clear and almost odourless solution. Since it is known that chloro-meta-cresol is an efficient disinfectant the same was to be

* Phenazone = phenyldimethyl-pyrazolone.

Zahn, Medizinische Klinik 1912, No. 47, p. 1913.

** Compare Merck's Reports 1910, 1911 and 1912.

expected of the above mentioned water-soluble combination. The pharmacological investigations undertaken by Zahn show that the preparation, administered by mouth or subcutaneously, displays locally as well as generally a surprisingly slight degree of toxicity, and in this respect is superior to cresol soap solution. At the same time its poisonous effect is very insidious, and this is of practical importance inasmuch as in the case of poisoning there is plenty of time for washing out the stomach and taking other protective measures. Introduced into the blood stream both phobrol and cresol soap solution are extremely poisonous already in small doses, and phobrol is even more toxic than the latter.

H. Kondring used phobrol for disinfecting the hands and site of operation and expresses a very favourable opinion of the value of the preparation. For quick disinfection he recommends the use of a mixture of 10 grammes of phobrol, 200 grammes of acetone and 790 grammes of alcohol (70 p. c.). For operations lasting a longer time, in which disinfection of the hands must be repeated after 25 or 30 minutes, a mixture of 1 part of phobrol and 100 parts of alcohol 70 p. c. (without acetone) is more suitable. When disinfected with this preparation the skin of the hands remains supple and smooth. The alcoholic solution is odourless and its use does not impart a disagreeable smell to the hands or operating room, even when large amounts are used.

J. S. Kalabin used a 0.5 p. c. aqueous solution of phobrol for antiseptic irrigations before and after delivery. He states that it is non-poisonous, is well borne and deserves wider recognition in gynaecological practice.

O. Wyss states that phobrol is especially suited for disinfecting sick rooms, for which purpose a 0.5 p. c. solution is employed; further, to cleanse the hands and other parts of the body soiled by secretions, e. g., in measles, diphtheria, scarlet fever, whooping cough, epidemic cerebrospinal meningitis, tuberculosis, etc. Handkerchiefs and cloths for bandaging may be disinfected in a solution of phobrol before being washed,

Kondring, Deutsche medizinische Wochenschrift 1913, No. 11, p. 513. — Compare also W. Bierast and A. J. M. Lamers, Zentralblatt für Bakteriologie 1913, I. Abt. Originale, Vol. 68, No. 2, p. 207.

Kalabin, Zentralblatt für Gynäkologie 1913, No. 44, p. 1627.

Wyss, Medizinische Klinik 1913, No. 43, p. 1767.

and water which has been used for washing or bathing can be disinfected by the addition of phobrol before being poured away.

Phosphorus.

Since infantile rickets is a disorder of metabolism in which, according to W. Gessner, on account of fat-hunger transformation of the foetal red bone marrow into ordinary yellow marrow cannot proceed in a normal manner, for its therapeutic treatment recourse should be had to an easily emulsified and quickly absorbed fatty compound, which is readily oxidised by the addition of phosphorus. These requirements are complied with in phosphorated cod-liver oil. It is capable of arresting the secondary demineralisation of the tissues and exerts a curative effect on the rickets. As is well known, phosphorated cod-liver oil and phosphorated oil have already for a long time played an important part in the treatment of rickets. On the other hand, P. Leubuscher's suggestion to use phosphorated oil (0.1 in 1000) in epilepsy is new. The author thinks that possibly similar physiological factors may cooperate in epilepsy as in tetany, in which phosphorus has a marked effect. The author has tried the use of phosphorated oil for two years, and has treated nine patients exclusively with this remedy. As these patients had already been in his charge in his home for several years the author is in a position to make an exact comparison of the number of fits before and during treatment by phosphorus. In some cases the improvement was insignificant, in others it was striking. In three patients the number of seizures was reduced by 30 or 40 p. c. The remedy was well borne by all the patients and during the whole duration of the treatment their body-weight remained practically unchanged. In some Leubuscher believes that he even saw a certain psychic improvement. The amount of improvement obtained was maintained after stopping the treatment without resorting to other drugs, only in the case of one patient the number of seizures rapidly increased to their former frequency after stopping the use of phosphorus. Although no positive cures could be achieved

Gessner, *Berliner klinische Wochenschrift* 1913, No. 15, p. 688.

Leubuscher, *Deutsche medizinische Wochenschrift* 1913, No. 11, p. 494.

by this treatment, nevertheless, phosphorus unquestionably had a marked influence on the fits, as all the patients treated were very severe cases. Whether this treatment has the same effect in mild cases remains to be seen.

Phosphotungstic Acid.

E. Pfeiffer undertook an investigation of the customary methods of estimating quantitatively the albumin in urine, in the course of which he found that the reagent suggested some years ago by Tsuchiya is a reliable substitute for Esbach's reagent (solution of picric and acetic acids), if suitable tubes are employed. He uses a somewhat more dilute solution than the one proposed by Tsuchiya. It is prepared by dissolving 1 gramme of phosphotungstic acid in 100 grammes of alcohol (96 p. c.) and 5 grammes of concentrated hydrochloric acid. With this reagent albuminous urines give a precipitate which gradually settles in cylindrical glass tubes (without a conical point) of 2 cm. in diameter and 14.5 cm. in length; after a certain time the upper layer of the precipitate is read. The glass tubes must be graduated empirically. The test is applied in the same way as with Esbach's reagent. However, it is considerably more reliable and its results are said to correspond with those yielded by gravimetric analysis. It has one drawback, i. e., forty-eight hours must elapse before the result can be read. A reading can be made after twenty-four hours, but the result must be calculated according to a table elaborated by the author. A preliminary test must be carried out before testing the urine to ascertain whether it contains much or little albumin, for the purpose of diluting it, if necessary. If on boiling a sample of the urine only large flakes separate out the urine may be employed without diluting; if the albumin is precipitated in large clumps the urine is diluted with water in the ratio of 1:1 or 1:2, until on boiling a flaky precipitate is produced. The fact must also be taken into account that if the urine is too much diluted the error is increased, and this should be avoided as far as possible. The urine or its dilution is mixed with an equal amount of the reagent in the graduated glass tube by gently rotating the tube; the author uses 10 c. c. of each.

Pfeiffer, Berliner klinische Wochenschrift 1913, No. 15, p. 677.

Tsuchiya, Merck's Report 1908, p. 112.

The mixture is then allowed to stand for forty-eight hours at a temperature of 12° to 15° R., whereupon the result is read. It is important that this temperature be maintained, and this point should not be overlooked.

To hasten the result the tube containing the urine and reagent may be placed in a Thermos flask in which it is kept for one hour at 30° R. The results obtained are less accurate, and several precautions must be observed which are fully described in the original paper.

Pilocarpine.

K. Herxheimer and H. Köster have undertaken therapeutic trials with pilocarpine in parapsoriasis. At first they wished to establish whether the secretion of sweat produced by pilocarpine would affect the subjective signs (itching); however, they found that the exanthema was influenced and they therefore continued the use of pilocarpine. In a case of parapsoriasis en gouttes in a girl, aged 19, they injected intramuscularly 0.01 gramme ($\frac{1}{6}$ grain) of pilocarpine hydrochloride at intervals of two or three days, without resorting to any other form of medicinal treatment. After each injection an outbreak of sweat occurred on the forehead, accompanied by redness of the skin, which gradually extended over the whole body. At the same time the patient experienced slight, transient nausea. Otherwise there was no disturbance of the general health and the action of the heart was not appreciably influenced. No visual disturbances occurred. On the other hand, after five injections the itching was relieved and an objective improvement in the exanthema was observed, consisting in desquamation. Further, involution of the infiltrate was evident in the papular efflorescences. On continuing this treatment a further improvement was obtained leading to the almost complete disappearance of the symptoms of the disease. Since the injections of pilocarpine were well borne in two cases further trials appear justified. This treatment should not be adopted in persons with severe cardiac changes or with signs of congestion of the lungs, and especially not in pregnant women. The authors state that otherwise the prolonged administration of pilocarpine is free from

danger provided the patients are kept under constant medical supervision. Should toxic symptoms occur an injection of 0.001 gramme ($\frac{1}{64}$ grain) of atropine sulphate is an effective antidote which immediately inhibits the action of pilocarpine.

In achylia pancreatica T. von Kern and E. Wiener gave acidol, pepsin and pankreon. However, with this treatment they observed the occurrence of severe diarrhoea which caused a loss of weight. They succeeded in entirely suppressing this unwelcome side-effect of the above mentioned treatment by systematically giving four to six subcutaneous injections of pilocarpine hydrochloride weekly. With this method of treatment of achylia pancreatica the pilocarpine directly stimulates the secretion of the pancreas, and this effect is reflexly increased by the acidol-pepsin. The increased pancreatic secretion enables a better utilization of food and consequently leads to a gain in weight.

A. Tachauer treated with pilocarpine a valuable young horse in which tetanus had developed after castration. In addition to local treatment with potassium iodide he injected subcutaneously 0.4 gramme (6 grains) of pilocarpine and 0.1 gramme ($1\frac{1}{2}$ grains) of physostigmine, and syringed the wound alternately with a solution of mercuric chloride and a solution of lysoform. The injection was repeated daily, and on the fourth day the improvement effected was so marked that no further injections were made. On the sixth day the wound began to heal.

Pinosol.

R. Polland states that pinosol* can be used as a substitute for oil of cade in various skin diseases such as prurigo, dry eczema, lichen urticatus, in the after-treatment of scabies, in fact in all irritative conditions of the skin. It can easily be rubbed into the skin in the form of 5 to 10 p. c. ointments or pastes, which relieve the itching and make the skin supple and smooth. Basing on his experience the author tried the following modification of Wilkinson's scabies ointment:

Kern-Wiener, Deutsche medizinische Wochenschrift 1913, No. 43, p. 2085.

Tachauer, Allatorvosi Lapok 1913, No. 9.

Polland, Österreichische Ärzte-Zeitung 1913, No. 3, p. 39.

* Compare Merck's Report 1912, p. 359.

Rp. Sulphur. præcip.	50 grammes	(1 ³ / ₄ oz)
Pinosol	100 „	(3 ¹ / ₂ oz)
Sap. moll.		
Adip.	aa 150 „	(5 oz)
Cretæ	15 „	(1 ¹ / ₂ oz)

This ointment proved very serviceable in the treatment of scabies; it is free from the unpleasant tar smell of Wilkinson's ointment and its use does not appear to produce any marked toxic symptoms, so that it can be used also in children's practice. A further great advantage of this ointment is the fact that it does not irritate the skin, and the addition of pinosol rapidly causes secondary inflammatory processes to heal. The ointment is also useful in various microphytic skin diseases, such as pityriasis versicolor and rosea, erythrasma, herpes tonsurans and eczema marginatum.

The author also employed pinosol in combination with Dreuw's chrysarobin ointment, according to the following formula:

Rp. Acid. salicyl.	10 grammes	(1 ¹ / ₃ oz)
Chrysarobin.		
Pinosol	aa 20 „	(2 ² / ₃ oz)
Sap. moll.		
Vaselin.	aa 25 „	(5 ⁵ / ₆ oz)

This ointment is especially useful in cases of psoriasis with extensive coalescence of lesions which are limited to a few parts of the body; it is less suitable for quite fresh cases with numerous disseminated small efflorescences. In extensive fresh cases pinosol is indicated in the form of a tar bath.

In seborrhœa of the scalp, especially in the oily forms, liquid pinosol soap for the hair may be used, which cleanses the scalp and gradually effects a return of the normal condition.

Pittysten*.

P. Schmidt has used preparations of pittysten with satisfactory results in various skin affections in veterinary practice. In acute and chronic eczema in dogs and cats he considers 10 p.c. liquid pittysten soap to be the best preparation, since the itching is relieved after washing a few times with the preparation and a cure is obtained within a surprisingly short

* Compare Merck's Report 1906, p. 195.

Schmidt, Berliner tierärztliche Wochenschrift 1913, No. 48, p. 859.

time, without any undesirable after-effects. The preparation also quickly relieves itching in the hind legs of horses. Further, a combination of pittylen and zinc sulphate yields good results in malanders. It is prescribed as follows:

Rp. Pittylen 75 grammes ($2\frac{1}{2}$ oz)

Zinc. sulph. 25 „ ($\frac{5}{8}$ oz)

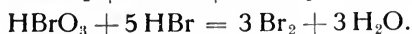
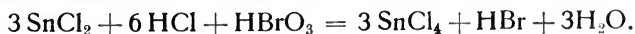
M. Sig.: Powder for malanders. To be applied as a dusting powder once or twice daily.

Polygonum Hydropiper.

Krawkoff's experience of liquid extract of Polygonum hydropiper in the treatment of hæmorrhages was reported in my last year's Report. The author's investigations were continued by L. A. Kaminskaja who obtained similar results. It therefore follows that this extract is a promptly acting hæmostatic. The cases treated by the authoress included bleeding at the menopause, bleeding due to uterine fibromyomata, chronic endometritis and displacement of the uterus, changes in the appendages and dysmenorrhœa. The preparation always displayed a good styptic action, and particularly in dysmenorrhœa an analgesic effect was noted. 25 to 40 drops were given three times daily.

Potassium Bromate.

F. Fichter and E. Müller have recently again recommended a practical method for the quantitative estimation of tin, which was elaborated by H. Zschokke but was not published in the literature. It is based upon the fact that in the presence of an excess of hydrochloric acid potassium bromate is converted into bromide by stannous chloride, and the bromide reacts upon the bromate with liberation of bromine. The following chemical process takes place:



The end-point of the reaction is recognizable by the appearance of free bromine, i. e., by a yellow coloration. The authors give the following instructions for carrying out the test: A

Krawkoff, Russkij Wratsch 1912, No. 7.

Kaminskaja, Wratschebnaja Gazeta 1913, No. 29.

Fichter-Müller, Chemiker-Zeitung 1913, No. 31, p. 309.

solution of tin, containing stannic, or stannous and stannic, salts, obtained by dissolving alloys of tin, tin or tin salts, is diluted so that it contains about 6 grammes of tin in 1000 c. c. To 20 c. c. of this solution in a flask 0.15 gramme of cut aluminium wire is added which causes a precipitate of metallic tin. Thereupon 30 c. c. of concentrated hydrochloric acid and 20 c. c. of water are added and after closing the flask with a stopper bearing a Bunsen valve the contents are heated to boiling. The tin goes into solution and a solution of stannous salt free from stannic salts is obtained. After cooling, it is immediately titrated with a solution of potassium bromate containing 2.7837 grammes of KBrO_3 in 1000 c. c., i. e., 1 c. c. corresponds to 0.00595 gramme of tin. The solution of potassium bromate is standardised by the iodometric method. This method is also applicable in the presence of phosphates.

Potassium Permanganate.

In view of the difficulty of properly treating severe burns, not only to obtain healing but also the best cosmetic result, a method proposed by S. C. Beck deserves recognition. He states that the moist treatment of burns is preferable to treatment with dry powders and ointments. For this purpose all the blisters are snipped and the raised epithelium is removed. The patient is then placed for five to thirty minutes in a bath with a temperature of 33° to $34^{\circ}\text{C}.$, the duration of immersion depending upon the patient's condition (action of the heart!). After the bath the patient is placed in bed, on waterproof sheeting, and the burnt parts of the skin are covered with several layers of gauze which has been dipped in a solution of potassium permanganate 1:4000 or 1:3000. To prevent evaporation the gauze is covered with waterproof material. About every half hour the gauze is moistened with a fresh lukewarm solution of potassium permanganate. If the patient's condition makes it feasible, in addition to this treatment he may take two potassium permanganate baths daily. For this purpose 3 or 4 grammes (45—60 grains) of potassium permanganate are dissolved in a child's bath full of water, or double this amount in the water of a large bath for adults. The patient remains

for thirty to forty minutes, or even longer, in this bath. To avoid unnecessary painful handling the patient is placed in the bath with the dressings on, which readily come off in the bath. The author selected potassium permanganate because it displays a powerful disinfectant action on account of its oxidising properties and removes the toxins from the burnt portions of tissue, without doing harm when used in the above dilution. The application of compresses is continued until an improvement is manifest in the patient's general condition. The object of this treatment is to allay the inflammatory symptoms, enable the unhindered discharge of the wound secretions, eliminate the toxic products produced by the burning, and to cleanse the surface of the wound. When this has been achieved treatment is continued by applying alternately an ointment containing 8 p.c. of amido-azotoluol* and a 5 p.c. cycloform ointment, to hasten the growth of epithelium. If hypertrophic scars or keloids should occur, recourse is had to fibrolysin** or to carbon dioxide snow***.

It is well known that the use of permanganates has been suggested for the treatment of Asiatic cholera†. To destroy the nitrous acid occurring in the organism in cholera L. Rogers made his patients drink in the place of any other beverage a 0.01 to 0.05 p. c. aqueous solution of calcium permanganate in such quantities that as much as 3 grammes (50 grains) of permanganate were taken in the course of two days. R. Emmerich ascribes the good effect of permanganate observed by Rogers to the conversion by organic substances present in the stomach of the permanganic acid into colloidal manganese dioxide hydrate, which oxidises the nitrous acid in statu nascendi to harmless nitric acid. Since the permanganates cannot be regarded as indifferent substances, he proposes to displace them by the use of colloidal manganese dioxide hydrate, which is easily prepared as a stable, dark-brown solution by allowing potassium permanganate to act upon a solution of gelatin. Since it is quite innocuous it can be drunk in any amounts by cholera patients.

* Compare Merck's Reports 1909—1912.

** Compare Merck's Reports 1904—1913.

*** Compare Merck's Reports. 1910—1912.

† Compare Merck's Report 1910, p. 134.

Rogers, British Medical Journal, 1910, II., p. 835.

Prophylacticum Mallebrein. (Mallebrein.)

The action of prophylacticum Mallebrein (a 25 p.c. solution of aluminium chlorate) is described in an exhaustive experimental work by W. Bierast and E. Ungermann. The authors ascribe the mechanism of the action of the preparation in diphtheria to its antitoxic properties, hence the preparation is useful in diphtheritic infections. On the other hand, it fails in infectious processes such as typhoid and anthrax, in which the disease is due more to an increase of the bacilli in the organism and in which the direct formation of toxins plays a secondary part. Tuberculous infection, too, was not appreciably influenced. In vitro, however, the preparation markedly reduces the specific action of tuberculin. The authors attribute a certain value to the fact that prophylacticum Mallebrein also acts at a distance from the actual site of its application, as they were able to demonstrate in the course of their pharmacological investigations.

K. Klare studied the action of prophylacticum Mallebrein in his sanatorium for tuberculosis, in which he had ample occasion to test it in the treatment of catarrhal conditions. His trials extended to pharyngitis, laryngitis, and especially to combating sub-febrile temperatures in tuberculous patients. In diseases of the pharynx he directed the patients to gargle three times daily with a 1 p.c. solution, in diseases of the larynx and lungs a 0.5 p.c. solution was inhaled thrice daily; in several cases both methods of application were combined. The bitter taste of the preparation, of which several patients complained, according to the author, is quickly removed by rinsing the mouth with water. Irritating cough only occurred when the patients breathed through the mouth while inhaling, and an irritating cough was never observed when they breathed through the nose. In agreement with Jarosch, Klare observed a beneficial influence to result from this treatment especially when the fever had been combated for some time. Thus he succeeded in bringing down the temperature to normal in patients in whom an elevation of temperature was constantly present prior to the day on which the use of prophylacticum

Bierast-Ungermann, Berliner klinische Wochenschrift 1913, No. 23, p. 1052.

Klare, Deutsche medizinische Wochenschrift 1913, No. 27, p. 1305.
Jarosch, Merck's Report 1912, p. 364.

Mallebrein was begun. In some cases, however, it failed to produce this effect, but this does not detract from a further trial of the preparation.

O. Steinmeyer, who also undertook a clinical study of prophylacticum Mallebrein, was unable to observe either a healing effect on the local affections treated with the preparation, nor any action at a distance from the site of its application. Similarly, in contradistinction to Wasmer's experience, obstinate elevation of temperature, hoarseness and toxic pulse were not influenced.

J. Schmidt states that prophylacticum Mallebrein is a useful remedy in veterinary practice, especially in the treatment of pleuropneumonia. To disinfect the pharyngeal mucous membrane a solution of 5 grammes of the preparation in 10 grammes of water is administered three times daily.

Proponal.

C. Stiatti prescribed this hypnotic* for a number of patients in his psychiatric practice, in whom the insomnia present had been unsuccessfully treated by other remedies, in some cases already for a prolonged period. He prefers to administer the drug in powder form, in which in his experience it is easier to administer to patients mentally affected. With few exceptions the hypnotic and sedative effect of doses of 0.25 to 0.5 gramme (4 to 7½ grains) was very satisfactory, which induces the author to draw the following conclusions:

Proponal is a hypnotic easy of administration, which acts already in small doses and produces a sound sleep lasting from five to seven hours. Sleep is induced in about an hour and a half after its ingestion. During the first hours of sleep circulatory and respiratory depression is observed, whereupon the normal condition again sets in. The drug also ensures complete rest during the daytime, without exhibiting any harmful secondary effects. It is excreted in very small amounts with the urine.

Steinmeyer, Beiträge zur Klinik der Tuberkulose 1913, Vol. 27, p. 221.

Wasmer, Merck's Report 1912, p. 363.

Schmidt, Mitteilungen des Vereins badischer Tierärzte 1913, No. 2; Berliner tierärztliche Wochenschrift 1913, No. 47, p. 836.

Stiatti, Note e Riviste di Psichiatria 1913, Vol. 6, No. 1.

* Compare Merck's Reports 1905—1908.

Protargol.

R. Reissmann describes some cases in which he used a 10 p. c. protargol ointment with very satisfactory results in the place of cauterisation with silver nitrate or copper sulphate. It proved very useful in a case of sclerosis in the vicinity of the coronary sulcus, which had existed for three weeks without showing any tendency to heal, in which it caused epithelialization within a short time. In a case of phimosis with gangrene, in which after the operation there were areas which discharged freely and showed only moderate granulation, the application of the ointment led within a short time to a decrease of the discharge and epidermization took place in the course of about two weeks. The ointment was used with equally successful results after an operation for whitlow and in a severe syphilitic sore.

L. Lilienthal and J. Cohn report on the abortive treatment of gonorrhœa in the male. In most cases they employed for this purpose solutions of protargol, to which they added a few drops of a solution of alypin nitrate to remove their irritant effect. On the first day they injected a 4 p. c. solution which was retained for four minutes in the urethra, and immediately repeated this procedure twice. On the second and third days a 5 p. c. solution was used. In this way on three consecutive days three injections daily of 8 c. c. of the above mentioned solutions were made, whereupon the abortive treatment was discontinued, whether it had proved successful or not. Frequently the discharge disappeared already by the second day, or it became more fluid and of a whitish colour. In 50 p. c. of the successful cases no gonococci could be observed under the microscope on the second day. If gonococci were still present on the third day, the authors regarded the case as hopeless, as they rarely succeeded in arresting the infection by giving the injections on the third day. With this treatment the desired result was obtained in about 50 p. c. of the cases, i. e., on the fourth day no clinical or microscopical signs were demonstrable. However, in those cases in which this method failed and other treatment had to be resorted to the duration of the gonorrhœa was appreciably shortened.

Further, this abortive treatment, even when it proved ineffectual, never caused any marked injury or complications.

Pyocyaneus-Protein Honl.

J. Lang has continued his clinical investigation of pyocyaneus-protein Honl* and was able again to confirm the high therapeutic value of this preparation. He used both pyocyaneus-protein Honl as well as anginol tablets in which the former is contained. Symptoms of inflammation in the mouth, pharynx and larynx were quickly alleviated by the use of pyocyaneus-protein, and several patients stated that the pains diminished already a few hours after its application. Out of thirty patients twenty-seven were cured within two days, and the remainder in three days. To ensure the preparation being active it must be kept as cool as possible, and in the consulting room only the amount required for immediate use should be kept.

Lang states that pyocyaneus-protein also proved useful in incipient peritonsillitis phlegmonosa, in which the author freely painted the inflamed spot as well as the lower pole of the tonsil and the region below the tonsil with the preparation once daily, and in severe cases twice a day. Forty-one cases were cured without operation, thirteen in two days, seventeen in three days, five in four days, three in five days, two in six days, and one in seven days. A combination of pyocyaneus-protein and mercuric chloride, whereby the latter was used as a gargle (0.1:1000), likewise yielded satisfactory results.

Pyocyaneus-protein may also be used with advantage in stomatitis aphthosa. Lang reports nine cases which were cured in from one to four days. He also advocates this treatment for the ulcers in the mouth which have burst, and in Vincent's angina, five cases of which were healed with pyocyaneus-protein in from four to six days.

Acute catarrh of the middle-ear with secretion, suppurative inflammation of the middle-ear and acute tubal catarrh are other promising indications for pyocyaneus-protein treatment, as Lang was able to observe in several cases.

Further, Lang obtained a prompt action with this prep-

Lang, Deutsche medizinische Wochenschrift 1913, No. 16, p. 748.

* Compare Merck's wissenschaftliche Abhandlungen No. 14.

aration in thirty-two cases of acute laryngitis; eighteen cases healed in from two to four days, twelve in from five to seven days, and three other cases in eight, eleven and twelve days respectively. Pyrocyanus-protein also yielded good results in chronic laryngitis, but the author's investigations in this direction are not yet completed.

Pyrocatechin.

K. Binder and R. F. Weinland describe a reagent worthy of notice in gas analysis. If alkali is added to a solution of ferrous sulphate and pyrocatechin under exclusion of the air, or of the oxygen of the air, and provided the iron salt used is free from oxide, a colourless solution is obtained which, according to the authors' statements, contains the alkali salt of a complex iron acid—pyrocatechin-ferrous acid. This mixture readily absorbs oxygen, whereby it assumes a deep red colour through the formation of the alkali salt of pyrocatechin-ferric acid, $H_3Fe(C_6H_4O_2)_3$. Hence this mixture may be used as a delicate test for gaseous oxygen. It must be prepared under exclusion of air; however, the solution is never colourless but always has a faintly reddish tinge as the ferrous sulphate is never quite free from traces of ferric salt. Exposed to the air the solution rapidly assumes a deep red colour, which begins from the top and extends downwards. To test mixtures of gases or fluids for the presence of free oxygen a suitable apparatus is required, since air must be excluded while carrying out the test. This reagent may also be used for the quantitative estimation of oxygen. For details of the method the original paper should be consulted.

Pyrogallol.

Among the caustics used in the treatment of lupus, pyrogallol, according to J. Jadassohn, is the most useful. In several cases he found that it yielded very good results, as a curative agent and also with regard to the cosmetic result, if its use is systematically carried out for a sufficiently long period. Pyrogallol treatment requires patience, but its application is simple. A 10 to 20 p.c. pyrogallol-vaseline is

Binder-Weinland, *Berichte der deutschen chemischen Gesellschaft* Berlin 1912, Vol. 45, p. 148 and 1113, and 1913, Vol. 46, p. 255.
Jadassohn, *Medizinische Klinik* 1913, No. 29, p. 1151.

used, which is spread upon linen or lint and applied to the part to be treated, and is kept in place by a suitable dressing. The affected part is cleansed every twenty-four hours with lukewarm oil and the application of pyrogallol is renewed. After a longer or shorter period, according to Jadassohn, ulceration of the tuberculous area sets in involving all the macroscopic manifestations. If this treatment should cause intolerable pain this is successfully combated by dusting anæsthesine on the parts before applying the pyrogallol ointment. As soon as the time has arrived when the ointment can no longer be used, recourse is had to preparations with a milder action such as boric acid vaseline, or moist compresses impregnated with boric acid solution, solution of aluminium acetate, or weak solutions of mercuric chloride; or treatment may be continued with ointments containing only 0.5 to 1 p.c. of pyrogallol. When the cauterised parts have been thrown off and the pains have subsided the application of a strong pyrogallol ointment is renewed and the above treatment is continued until epithelialization of the lupous areas sets in. This treatment is also suited for tuberculous affections of the lymph glands in which the skin is involved, and for tuberculosis of the bones with sinus formation. In these cases the urine should be watched and not too large areas should be treated at the same time, otherwise a general toxic action of pyrogallol may manifest itself.

Quinine.

Lenzmann already suggested the use of quinine in the treatment of syphilis, and recently J. Schereschewsky has used it in this disease. However, whereas Lenzmann administered quinine intravenously, Schereschewsky found that quinine, applied in the form of a 40 p.c. quinine ointment, possesses a considerable prophylactic value. He undertook experiments on monkeys which were infected with syphilitic material on the whole of the frontal plane, whereupon one half of the infected surface was treated with a quinine ointment. Even when the ointment was applied several hours after the infection, on the appearance of the primary manifestations in

the animals these occurred only on the side which had not been treated with the ointment. The author believes that the use of quinine ointment should prove successful also in human practice.

Z. Donogany reports his experience with the quinine treatment of acute tonsillitis, proposed by Jordan. He obtained the best results by giving 1 gramme (15 grains) of quinine in two portions in the evening between 7 and 7.30 p. m.; by dividing the dose in this way he was able to prevent the occurrence of ringing in the ears. As soon as the patient showed no fever on the following morning and evening the quinine was stopped; only in the presence of slight hyperæmia or difficulty in swallowing another dose of 0.5 gramme ($7\frac{1}{2}$ grains) is given. If fever again occurs, or if the other tonsil becomes affected, the dose of 1 gramme (15 grains) is repeated. With this treatment most cases were cured in one or two days. However, the author saw a few cases in which no cure was effected, but an abscess formed in or on the tonsil, or Vincent's angina or diphtheria set in. Some cases of follicular tonsillitis, in which in addition to slight local severe general manifestations were present, healed only in the course of eight days; the majority of cases, however, reacted promptly to this treatment.

In malaria E. E. Waters has used the so-called "cinchona sulfruge" with successful results in the place of quinine sulphate. The author states that this preparation, which consists of all the crystalline and amorphous alkaloids contained in cinchona bark, is more effective than pure quinine. He also tested the action of the amorphous alkaloid, the substance remaining in the mother-lye after the separation of the crystalline alkaloids, and he found that this was still more effective. Whereas 1.8 to 3.6 grammes (27—54 grains) were required to combat the fever, 1 gramme (15 grains) of the amorphous alkaloid proved sufficient. The amorphous alkaloid is also said to be free from secondary effects. In the place of cinchona febrifuge the well-known quinetum might be used, and quinoidin instead of the amorphous alkaloid. (Compare Merck's Index 1910, p. 78.)

Radish.

The radish, *Raphanus sativus* L. (griseus and niger), is a fairly old and popular remedy for cholelithiasis, therefore some authoritative information on its use should prove interesting. Grumme assumed that radishes, or the juice of radishes, either influence the secretion of bile in such a way that the anomalies and congestion which lead to the formation of gall-stones are removed, or that the radish contains substances which prevent or suppress the inflammatory manifestations which cause the formation of gall-stones. He has made trials with the juice of radishes for twelve years and has obtained such satisfactory results that he advocates a more general trial of his method of treatment, which is carried out as follows:

White or black radishes are peeled, crushed in a suitable apparatus and the juice expressed. If the treatment is begun during or after an attack, the patient is made to drink on the first day half a cupful (100 c. c.) [$3\frac{1}{2}$ oz] of the juice, then a whole cupful and later two cups (400 c. c.) [14 oz] daily. This amount is taken daily for two or three weeks, whereupon the dose is gradually decreased, until half a cupful is taken three times a week. This treatment is continued for six to eight weeks. When this treatment is repeated one cupful of juice daily is taken in the beginning, then half a cupful daily and later half a cupful every second day.

Grumme did not adopt this treatment in unsuitable cases, i. e., cases complicated with empyema, or cases in which during the period of freedom from attacks the painfulness to pressure of the gall-bladder persisted, or in which the general health or appetite were impaired. In a series of cases he succeeded in effecting permanent freedom from attacks by his method.

Since the active principles of the radish are not known and it cannot well be assumed that they cause solution of the stones present, Grumme attributes the therapeutic value of the radish to its influence on the secretion of bile, whereby it prevents an increase of the cholesterin stones. In addition, under the influence of radish juice the bile is probably endowed with antiphlogistic properties, so that the biliary engorgement produced by inflammatory swellings of the mucous

membranes either subsides or disappears, and by this means a condition of latency is established.

H. Engels points out that the popular conception of the value of radish juice as a useful remedy for gall-stones has been shared by experienced practitioners, and that, *inter alia*, already C. Gerhardt alluded to it in his clinical lectures. He is able to confirm Grumme's findings*.

Ragit Nutrient Media.

A very favourable opinion of the ragit nutrient media already described in these Reports** is expressed in a paper by H. Richter. For use in bacteriological laboratories they have the great advantage that nutrient media can be prepared in a far shorter time and with much less trouble than the customary gelatin and agar nutrient media. The results obtained by their use are in no respect inferior to those yielded by other nutrient media, and are often superior. Further, their use ensures the preparation of nutrient media of constant composition. Richter states that the chemical composition of the ragit preparations is eminently satisfactory; their neutral reaction and the small content of carbohydrates affords the necessary latitude to alter the reaction, or increase the content of carbohydrates, so that the ragit preparations offer an excellent basis for easily preparing special nutrient media.

Richter states that the ragit-Endo tablets yield the best Endo nutrient medium. They are also well suited for differentiating *Coli* and typhoid bacilli. Ragit nutrient media should prove especially useful in water analysis, since their use yields nutrient media of uniformly constant composition, thereby ensuring greater uniformity of results.

The "ragit serum" recommended by E. Marx is a dry preparation which marks a further advance in bacteriological technique. It is used for preparing Loeffler's serum, and presents the great advantage of entirely doing away with the necessity for obtaining, or storing, liquid serum. Ragit serum

Engels, *ibidem* 1913, No. 34, p. 1379.

* A preserved radish juice has been placed on the market under the name of "Cholosan". (Compare *Pharmazeutische Zentralhalle* 1913, p. 1133.)

** Compare Merck's Reports 1911 and 1912.

Richter, Dissertation Lausanne 1913.

Marx, *Zentralblatt für Bakteriologie (Originale)* 1913, Vol. 72, No. 3.

occurs as a powder and consists of a mixture of ragit agar* and dry genuine albumin.

To prepare Loeffler's serum 13.3 grammes of ragit serum are mixed with 100 c.c. of tap-water in a mortar—the dry powder is first rubbed down to a smooth paste with a little water whereupon the remainder of the water is gradually added, as well as 5 c.c. of glycerin. The mixture is poured into Petri dishes or into test-tubes and sterilized. As a rule, small laboratories are not provided with a special cupboard for sterilizing Loeffler's serum, in which it is also allowed to solidify, therefore the mixture may be treated in an appropriate manner in a steam steriliser.

On this nutrient medium diphtheria bacilli usually show a colourless and finer growth than upon the original Loeffler serum. This nutrient medium may also be used for the cultivation of other bacteria requiring albumin for their growth; in this case, however, as a rule, the glycerin is omitted, or a smaller amount is added.

Ristin.

The statements of Neuberger and Tollens regarding this new remedy for scabies are fully confirmed by Boltens-tern, A. Roth, Fischer, F. Moses and F. Treitel. Moses directed his patients to apply ristin daily, to which he added a small amount of castor oil to make it somewhat sticky so that it should adhere better. Living mites were frequently found after the first application, but in some cases no living mites were found even after this brief treatment. As a rule, after the second application all the mites were killed, in every case after four or five applications, and this number sufficed to effect a cure. Among a large number of cases the author observed irritation of the skin in one instance only, and this case had already exhibited hypersensitiveness to Peru balsam. None of the other cases showed

* Compare Merck's Reports 1910 and 1911.

Neuberger-Tollens, Merck's Report 1911, p. 377.

Boltens-tern, Deutsche Ärzte-Zeitung 1912, No. 1, p. 2.

Roth, Bör-è-Bujakortan in Budapesti Orvosi Ujsag 1912, No. 3.

Fischer, Zeitschrift für ärztliche Fortbildung 1912, No. 23.

Moses, Medizinische Klinik 1913, No. 14, p. 544.

Treitel, Therapie der Gegenwart 1913, No. 2, p. 94. — Ärztlicher Zentral-Anzeiger 1913, No. 23.

even the slightest alteration of the skin, indeed the desiccation of the burrows of the mites was so slight that they appeared practically uninfluenced, and the fact that a lasting cure had been effected was evidenced solely by finding only dead mites and by the prompt cessation of the itching. For use in hospitals, where the treatment of scabies is principally carried out, Treitel recommends in the place of pure ristin a mixture of 50 grammes of ristin, 25 grammes of glycerin and 125 grammes of alcohol. Compared with the older remedies this mixture has the advantage, which is a feature of ristin, that it does not soil the linen and on account of its being free from smell does not incommode the patients or their attendants. Treitel emphasises the necessity for thoroughly rubbing the ristin into the skin until it appears to be dry. Boltenstern and Fischer obtained equally satisfactory results.

Sandal Wood Oil.

Gonosan* occupies a leading position among the preparations of sandal wood oil, and this is again evidenced by the publications of Geissler, Perrin and Pohl. According to Geissler a great advantage of this useful antigonorrhœic lies in the fact that it shortens the duration of the disease, the purulent discharge is quickly replaced by a mucous discharge, and the gonococci rapidly disappear from the discharge. In addition, it allays the irritation and the pains in that by its use the patient is not troubled by painful erections, strangury and scalding during micturition. It also appears to prevent complications. Further, it is not nauseating and is readily taken by the patients; it does not irritate the kidneys and does not cause gastric derangement. However, Geissler states that its good action is displayed only when it is given at the earliest possible moment, and its beneficial influence on the course of the disease becomes less apparent the later its administration is begun. In old-standing cases, and in such which have become chronic, an immediate result cannot be expected, and in these cases external treatment is indicated. In addition, the author points out that the internal use of gonosan should be combined with external treatment, and for this

* Compare Merck's Reports 1902—1911.

Geissler, Reichs-Medizinalanzeiger 1913, No. 2, p. 35.

Perrin, La clinique 1913, No. 29, p. 452.

Pohl, Therapeutische Monatshefte 1912, No. 12, p. 874.

purpose he advocates injections of protargol solution. Perrin prefers injections of a 0.1 p. c. solution of syrgol. In acute cases of urethritis he prescribes 16 to 20 gonosan capsules (0.3 gramme each) daily, to be taken in three or four portions.

Pohl has investigated a number of balsam preparations according to Winternitz's method, as modified by himself, and he found that pure sandal wood oil and gonosan acted well, whereas several other commercial preparations of sandal wood oil, per se or in combination with other drugs, proved ineffective or displayed only a slight action. He states that kava resin undoubtedly promotes the antiphlogistic effect of the balsams.

G. Haedicke reports on another preparation of sandal wood oil — kawakawin. It is a mixture of oil of sandal wood, kava resin and hexamethylenetetramine, and its therapeutic value is stated by the author to be equal to that of other preparations of sandal wood oil.

Salvarsan.

In salvarsan treatment the technique plays a very important rôle, especially the preparation of the solutions used for intravenous injection, leaving out of the question the indications for its use. For instance, apart from the well-known "water-error", Matzenauer draws attention to the "glass error", which may be responsible for some of the secondary effects seen when injecting salvarsan, if these cannot be ascribed to decomposition of the solution of salvarsan or to the water employed. The author attributes the "glass error" to absorption of alkali from the glass of the vessels used for keeping the water, or in which the physiological salt solution has been sterilized. It is not always productive of unwelcome effects, but may occasionally give rise to such, and should therefore be taken into account in preparing solutions of salvarsan. The preparation of salvarsan solutions has been made the subject of numerous communications, in which full particulars will be found*.

Haedicke, Allgemeine medizinische Zentral-Zeitung 1913, No. 16, p. 190.
Matzenauer, Wiener klinische Wochenschrift 1913, No. 11, p. 406.

* Compare Pharmazeutische Zeitung 1913, No. 58, p. 571 and No. 61, p. 603 and also under "Technique" in the bibliography given below.

The use of concentrated solutions of salvarsan for intravenous injection has aroused considerable interest, and is dealt with, *inter alia*, by Lube, Zimmern, Finckh, Dreyfus and Strauss. After Stern, Strauss and others had obtained good results by the use of concentrated solutions of neo-salvarsan, the above cited authors proceeded to try the use of concentrated solutions of salvarsan. Zimmern injected 8 to 10 c. c. of a 5 p. c. solution by means of a Record syringe, but in spite of the most careful technique he saw secondary effects such as fever, venous pains and vomiting. The experiences of other observers were more satisfactory. After exhaustive trials Dreyfus found that the injection is best tolerated if the dose is administered in 30 c. c. of water, using a syringe with a capacity of 35 c. c., whereby special care must be taken in preparing the solution of salvarsan and in adding the alkali; the injection should be made very slowly. The author summarises his experiences as follows: The injection of 0.1 to 0.5 gramme of salvarsan in about 35 c. c. of twice distilled water (highest concentration $\frac{5}{4}$ p. c.) has several advantages over the method hitherto adopted of infusing the salvarsan in 150 to 250 c. c. of fluid, in that the subjective and objective reactions are far slighter than when a large amount of fluid is infused. A proper course of salvarsan treatment consists of twelve to fifteen injections, given over a period of several weeks. The small amount of fluid injected undoubtedly subjects the circulation to far less strain than is the case when 250 c. c. of fluid are introduced; further, diuresis is not stimulated to the same extent by these small amounts of fluid, and therefore the salvarsan is retained longer in the organism (Zimmern). To dissolve the drug only absolutely pure water is required, physiological salt solution is not necessary. Sterilisation of the glass vessels can be accomplished by boiling for twenty minutes, whereby the hitherto customary tedious and complicated sterilisation in the drying chamber is obviated. This means a considerable simplification and saving in time for the practitioner who has to make several consecutive injections, and for nervous

Lube, *Dermatologische Zeitschrift* 1913, No. 1.

Zimmern, *Münchener medizinische Wochenschrift* 1913, No. 20.

Finckh, *Medizinische Klinik* 1913, No. 13.

Dreyfus, *Münchener medizinische Wochenschrift* 1913, No. 42.

Strauss, *Dermatologische Wochenschrift* 1913, No. 14.

patients an injection made with a syringe is a far less formidable procedure than having to submit to an infusion. The action on the kidneys is the same whether a concentrated or dilute solution is employed, nevertheless, in marked nephritis salvarsan, if used at all, should be given only in dilute solution. On the other hand, in syphilitic affections of the organs of circulation small doses in concentrated form are indicated. The author states that the use of concentrated solutions presents one drawback in that the intravenous injection demands faultless technique, since infiltrations and perivenous tissues are naturally more painful with concentrated solutions and may prove more dangerous (thrombosis) than with dilute solutions. Such incidences are not due to the method, but to want of experience.

The combined use of salvarsan and mercury is discussed by Sachs, Boas, and others. According to Boas, the early treatment of syphilis consists in excision of the sclerosis, a combination of mercurial preparations (injections of 10 p. c. mercury salicylate, 2 p. c. imido-succinate of mercury, 5 p. c. asurol, inunctions with mercurial ointment, and the internal administration of mergal and preparations of iodine) and salvarsan. In early cases this treatment should be continued intermittently with strict individualization and constant control by the Wassermann reaction. The author states that compared with the use of salvarsan alone, this combined treatment yielded far better results. Boas's results lead to similar conclusions.

H. Müller makes some interesting statements regarding the permanency of the results of abortive treatment with salvarsan, which fully establish the high value of this method. Further, the author draws attention to the use of intramuscular injections of joha which, with proper technique, are indicated in those cases in which infusion into a vein cannot be undertaken. To obtain a favourable result with this method of application it is essential that the patients be kept at least two days in bed in order to prevent sinking of the deposit. According to Weck the action of intramuscular in-

Sachs, Wiener klinische Wochenschrift 1913, No. 46.

Boas, Münchener medizinische Wochenschrift 1913, No. 47.

Müller, Münchener medizinische Wochenschrift 1913, No. 8.

Weck, Archiv für Schiffs- und Tropenhygiene 1913, Vol. 17, p. 559.

jections of joha* in syphilis, frambœsia and tropical ulcers of the leg is equal to that of salvarsan infusions, whereas in relapsing fever it sets in too late or not at all. On the other hand, Scherschmidt considers the intravenous injection of salvarsan to be more effective in frambœsia.

With regard to the contra-indications to salvarsan treatment Rindfleisch states that when status thymo-lymphaticus is suspected salvarsan should be used with the utmost caution, especially in children. For instance, in about 70 p.c. of the cases of Graves's disease this anomaly is present, therefore the author is of opinion that the presence of Graves's disease is an absolute contra-indication to the use of salvarsan.

The excellent effect of salvarsan in pleuro-pneumonia in horses is now fully established**; it may be mentioned that Wolf also tried it in cerebrospinal inflammation (Bornasche Krankheit) with negative results. For further indications the following bibliography should be consulted.

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* Compare Merck's Reports 1911, p. 380, and 1912, p. 378.

Scherschmidt, Archiv für Schiffs- und Tropenhygiene 1913, Vol. 17, p. 552.

Rindfleisch, Berliner klinische Wochenschrift 1913, No. 12.

** Compare Merck's Report 1912, p. 379.

Wolf, Zeitschrift für Veterinärkunde 1913, No. 12.

1913, Vol. 5, p. 318. — Igersheimer, Münchener medizinische Wochenschrift 1913, No. 11, p. 610. (Local use in Keratitis parenchym.). — Vandegrift, Medical Record 1912, October 26, (Keratitis interstitialis). New York Medical Record 1912, October 26.

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Ziegel, Medical Record 1913, p. 1124.

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Assmy, Kyritz, Archiv f. Schiffs- und Tropenhygiene 1913, Vol. 17, p. 217.

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Vincent's Angina:

Anglade, *Progrès médical* 1913, No. 7. — Citron, *Berliner klin. Woch.* 1913, No. 14, p. 627.

Scarlet Red, Medicinal. (Amido-Azotoluol, Pellidol.)

For the treatment of ozæna and atrophic rhinitis Jacobs recommends a 5 p. c. suspension of scarlet red* in mucilage of acacia or in mucilage of tragacanth, which adheres well to the nasal mucous membrane. Before applying this preparation the mucous membrane must be freed of crusts, and this procedure is best assisted by the use of solvent sprays. The suspension of scarlet red is then applied on a pledget of cotton wool to the nasal mucous membrane, at first every second or third day and later at longer intervals, care being taken to ensure its application over the whole surface. With this treatment the author obtained an improvement after two or three weeks; the foul odour diminished or disappeared entirely, the crusts were removed with greater facility, and the mucous membrane appeared less atrophic and anæmic.

M. Stark used scarlet red with very satisfactory results in the treatment of wounds which refuse to heal, since he found that granulation and epithelialization quickly set up under the action of this drug. However, as a rule, this good effect is only displayed in clean wounds, and in not too extensive wounds; in extensive wounds exuberant granulation sets up

Jacobs, *Semaine médicale* 1913, No. 26, p. 307.

* Compare Merck's Reports 1908—1912.

Stark, *Urologic and Cutaneous Review* 1913, No. 1.

in the middle of the wound whereby epithelialization is delayed. In the latter only the margins should be treated with scarlet red ointment (not stronger than 10 p. c.) and after twenty-four hours an indifferent ointment should be applied. In the meantime the central parts of the wounds are cauterised with silver nitrate. J. Staige Davis, in agreement with Stark, states that injury from the use of scarlet red need only be feared if it is applied for too long a period. In a case described in detail the use of a 4 p. c. amido-azotoluol ointment after skin-grafting caused excessive thickening of the Thiersch's graft, whereas this assumed a normal thickness under treatment with compresses of salt water. This observation is in agreement with N. Dobrowolskaja's experience. This author divided granulating wound surfaces into two equal halves, and treated the one half for one day with scarlet red ointment and then for two days with an indifferent ointment; to the other half an indifferent ointment only was applied. With one exception all the cases treated showed that the application of amido-azotoluol or scarlet red does not yield any better results than the use of indifferent ointments and dry aseptic dressings.

K. Scheele states that animal experiments and clinical investigation have demonstrated that scarlet red and amido-azotoluol, used in the form of ointments, may be considered for clinical purposes to be non-toxic. He is of opinion that amido-azotoluol unquestionably has a more powerful and quicker action. It is true that in animals it causes slight irritation of the kidneys, however, in amounts which are not used for clinical purposes. Cases of idiosyncrasy occur even when using an 8 p. c. amido-azotoluol ointment, as is apparent from a paper by H. M. Lyle. The author reports a case of an extensive burn which was treated with this preparation. As secondary effects he observed headache, gastralgia, vomiting, cyanosis of the lips, loss of force of the pulse and elevation of temperature.

G. Berlatzky is extremely satisfied with the action of

Davis, *Annals of Surgery* 1913, Vol. 58, p. 451.

Dobrowolskaja, *Beiträge zur klinischen Chirurgie* 1913, Vol. 83, No. 1.

Scheele, *Dissertation* Berlin 1912.

Lyle, *Deutsche Medizinisch-Zeitung* 1913, No. 10, p. 167.

Berlatzky, *Praktitscheskij Wratsch* 1913, No. 31.

amido-azotoluol in the treatment of burns. Especially in large burns he advises a trial with the preparation before resorting to skin-grafting, as in his experience it proved exceedingly useful. C. Egger states that it proved very useful also in chronic middle-ear suppuration, although it failed in some cases. Further, it is of service in the after-treatment of radical mastoid operation. In these cases the author applied iodoform gauze during the first fortnight, then epidermol gauze, and every second day, after thoroughly cleansing with alcohol, he applied a thin layer of a mixture of 1 part of amido-azotoluol and 9 parts of powdered boric acid. This treatment occasionally caused a slight irritation of the granulations.

C. Decker prefers pellidol* to promote epithelialization since its use is cleaner and it appears to act better. Haass, B. Bendix, Th. Hoffa and A. Hoffmann also report on the use of this preparation.

Bendix tried a 2 p. c. pellidol-vaseline in various forms of eczema in children and came to the conclusion that it rapidly alleviates the inflammatory manifestations, while the crusts are quickly thrown off. In weeping eczemas it stops the discharge, and in scaly eczemas desquamation ceases; moreover in all eczemas the itching is relieved. The ointment is spread on gauze and then applied. After about six to eight hours the ointment has been absorbed by the skin and the crusts are partly thrown off. After two or three applications of the ointment a wound forms on the surface of the skin which is soon followed by epithelialization. The author acknowledges that pellidol ointment occasionally fails; however, he states that he has never seen any other remedy display a so rapid and permanent healing effect on chronic, especially scaly eczema of the face in children. Hoffa reports equally satisfactory results. He states that intertrigo offers a specially promising field for pellidol treatment. Finkelstein found

Egger, Dissertation Berne 1913.

Decker, Medizinische Klinik 1912, p. 1990.

* Compare Merck's Report 1912, p. 390.

Haass, Wochenschrift für Therapie und Hygiene des Auges 1913, Vol. 16, p. 329.

Bendix, Therapeutische Monatshefte 1913, No. 5, p. 350.

Hoffa, Deutsche medizinische Wochenschrift 1913, No. 25, p. 1209.

Hoffmann, Berliner tierärztliche Wochenschrift 1913, No. 20, p. 363.

it very serviceable in the ulcerous affection of the gluteal skin designated by him as dermatitis papulo-vesiculosa glutealis. Surprisingly rapid epithelialization occurred in a case of extensive syphilitic rhagades on the palms of the hands and soles of the feet with deep cracks of the skin in which in addition to pellidol mercury iodide was also prescribed. In the treatment of wounds pellidol, and its combination with iodolen, so-called azodolen*, yields the same effects as scarlet red and amido-azotoluol. The fact that it does not stain and its solubility in the customary ointment bases, whereby a 2 p. c. pellidol ointment displays the same action as an 8 p. c. scarlet red ointment, constitute an advantage over scarlet red.

Haass obtained good results with pellidol ointment in eczematous inflammations of the cornea; and in obstinate recurring loosening of old corneal scars with a solution of pellidol and atropine in oil. On the other hand, pellidol treatment appears to be contra-indicated in uncomplicated corneal infiltrations with relatively intact epithelial covering of the cornea, and in superficial epithelial abrasions of the cornea. Pellidol (and likewise azodolen) proved ineffective in infectious conjunctival catarrhs, especially in diplobacillus catarrh, and this does not point to the preparation possessing any marked bactericidal power.

Hoffmann discusses the use and value of scarlet red, pellidol and azodolen in veterinary medicine. He states that these preparations are useful in the treatment of eczemas and wounds.

Scopolamine.

Fühner reports some interesting observations on the combined action of morphine and scopolamine, which he made in the course of pharmacological investigations. He found that the narcotic action of morphine is intensified by scopolamine, and this effect may be explained as follows: Indifferent narcotics already effect an increase of the morphine action, possibly through the second narcotic increasing the solubility of the alkaloid at the seat of its action in the central nervous system. Summation of action also takes place if absorption from the site of application is improved by the attendant substance.

* Compare Merck's Report 1912, p. 391.

Fühner, Deutsche medizinische Wochenschrift 1913, No. 3.

The same effect must be manifested if the elimination of the first substance is impeded by the second substance. Scopolamine inhibits glandular secretion in the body, and possibly it intensifies the action of morphine by acting in the above described manner. In dealing with a substance which is readily destroyed in the organism, as is the case with morphine, it may be assumed that its action might be increased by a second narcotic retarding the rapidity with which it is destroyed in the body. According to Fühner, the mechanism which is responsible for increasing the action in this case, and with other mixtures of drugs, is doubtless amenable to experimental demonstration.

M. Cloetta deals with the question whether l-scopolamine (the scopolamine of the German pharmacopœia), in contradistinction to Cushny's view, really has a more powerful action than racemic scopolamine, as had been maintained by Hug. Basing on theoretical considerations and on clinical experience he comes to the conclusion that both substances do not display the same action on the central nervous system, and that l-scopolamine has a more powerful action.

R. Kümmell describes the advantages and drawbacks of morphine and omnopon-scopolamine anæsthesia in operations on the eye. He states that it is a great advantage that the operation can be performed without a mask, and that the induction of anæsthesia is not only usually successful but is also ideal, so that the operation can be safely terminated without interruption. On the other, a drawback of this method is that individualization of the dosage is necessary, and that in the event of toxic symptoms supervening the drug injected cannot be quickly removed from the body, whereas this is accomplished within a short time on interrupting inhalation anæsthesia.

M. Kleimann states that scopolamine-omnopon anæsthesia, or the induction of anæsthesia by scopolamine and omnopon, has proved very effective in gynecological operations. The author's method consists in giving the patient on the evening before

Cloetta, Archiv für experimentelle Pathologie 1913, Vol. 71, p. 290.

Compare Merck's Report 1912, p. 391.

Kümmell, Klinische Monatsblätter für Augenheilkunde 1913, Vol. 51, p. 390.

Kleimann, Russkij Journal akutscherstwa i shenskich bolesnej 1913, Vol. 28, p. 99.

the operation 0.3 to 0.5 gramme (5—7½ grains) of veronal, and three quarters of an hour to one hour before the operation an injection of 0.04 gramme ($\frac{2}{3}$ grain) of omnopon and 0.0004 gramme ($\frac{1}{160}$ grain) of scopolamine hydrobromide. The operation is performed under oxygen-ether or oxygen-chloroform anæsthesia. The injection necessitates the use of a smaller amount of ether or chloroform and consequently pulmonary complications are rarer. The oligopnoea observed in a few cases is attributed by the author to the scopolamine alone. This is not in keeping with Michelsson's experience; this author used scopolamine-morphine (0.0005 gramme [$\frac{1}{125}$ grain] of scopolamine hydrobromide and 0.01 gramme [$\frac{1}{6}$ grain] of morphine hydrochloride) in several thousands of cases without ever observing the slightest disturbance of respiration, whereas when morphine was tentatively replaced by omnopon cyanosis and irregular respiration frequently occurred.

M. Nentwig considers omnopon-scopolamine mixed anæsthesia a valuable combination, since scopolamine and omnopon, administered in small doses, eliminate to a great extent the risks attending anæsthesia. Hence this method of inducing anæsthesia may be adopted in older persons with debilitated organs, without increasing the dangers attending the operation. It is especially to be recommended in cases where deep anæsthesia is not required, e.g., in abdominal surgery, but it is not indicated in children under sixteen years of age and in drinkers. Scopolamine should be injected in two separate doses, with an interval between each injection. M. Mehlhorn adopts a similar procedure. About two hours before the operation he injects subcutaneously, or intramuscularly, 0.02 gramme ($\frac{1}{3}$ grain) of omnopon and half an hour later 0.02 gramme ($\frac{1}{3}$ grain) of omnopon and 0.0005 gramme ($\frac{1}{125}$ grain) of scopolamine hydrobromide, in robust individuals 0.0006 gramme ($\frac{1}{100}$ grain). Ether was the anæsthetic used, in some cases a little chloroform was used for inducing anæsthesia; 40 to 175 grammes of ether were required. In juveniles and in aged persons, and also in midwifery cases, the author deprecates the use of scopolamine and prefers the use of omnopon alone. He lays stress upon the post-operative action of omnopon-sco-

Michelsson, Zentralblatt für Chirurgie 1913, No. 18, p. 695.

Nentwig, Archiv für klinische Chirurgie 1913, Vol. 102, No. 4.

Mehlhorn, Deutsche medizinische Wochenschrift 1913, No. 45.

polamine, consisting in a state of rest resembling sleep and lasting for seven to nine hours. Vomiting is said to be a rare occurrence; on the other hand, peristaltic movements of the intestines and flatus occur within a surprisingly short time, and this action may be assisted by the application of warmth to the abdomen.

According to Bürgi, the use of omnopon, in combination with scopolamine, has the advantage over morphine that vomiting does not occur so easily, and further that it exerts less influence on the respiratory centre. A combination of scopolamine and omnopon is useful for producing dawning sleep (Dämmer-schlaf), as a preliminary to inhalation anæsthesia, and as an adjuvant to local, spinal or sacral anæsthesia. For a dose the author advises, for robust persons, 0.04 gramme ($\frac{2}{3}$ grain) of omnopon and 0.0004 to 0.0006 gramme ($\frac{1}{160}$ — $\frac{1}{100}$ grain) of scopolamine hydrobromide; for juveniles and debilitated individuals, and patients with disturbances of respiration, these amounts should be considerably reduced. To abolish labour pains the author recommends the use of 0.02 gramme ($\frac{1}{3}$ grain) of omnopon and 0.0002 gramme ($\frac{1}{320}$ grain) of scopolamine hydrobromide. On the other hand, H. Hölder states that it is not possible to establish any rules capable of general application regarding the dosage, and, according to her experience, the absence of any control on the action is due not only to its varying absorption in different individuals, but also to the fact that its power of absorption constantly varies even in the same person and therefore cannot be controlled. The best time for operating would be the moment when all has been absorbed and nothing eliminated; however, it is impossible to determine this moment, apart from the fact that elimination may begin already prior to its complete absorption. Therefore, since it is not possible to determine with certainty the dosage in each individual case by giving a tentative injection, the authoress advises that a dose of 0.0006 gramme ($\frac{1}{100}$ grain) of scopolamine should not be exceeded, and in aged and debilitated persons only half this amount should be given.

For combined scopolamine anæsthesia H. Reichel advocates the use of narcophin in the place of omnopon, since

Bürgi, Deutsche Zeitschrift für Chirurgie 1913, Vol. 125, p. 211.

Hölder, Zentralblatt für Gynäkologie 1913, No. 11, p. 380. Compare

H. Sieber, ibidem 1913, No. 14, p. 496.

Reichel, Münchener medizinische Wochenschrift 1913, No. 12, p. 638.

he has seen severe disturbances of respiration when using omnopon and omnopon-scopolamine. He has employed scopolamine-narcophin with gratifying results in a large number of cases of operation for goitre. He never exceeded a dose of 0.03 gramme ($\frac{1}{2}$ grain) of narcophin. H. Hinterstoisser also injected doses of 0.03 gramme ($\frac{1}{2}$ grain) of narcophin and 0.0005 gramme ($\frac{1}{125}$ grain) of scopolamine hydrobromide with satisfactory results; however, he does not consider narcophin a harmless substitute for morphine for combined anæsthesia. His paper, which does not lend itself to brief abstraction, also contains some interesting data regarding morphine poisoning and its treatment, and should be consulted by those interested in this subject. With regard to the favourable influence of combined injections of scopolamine and opium alkaloids on labour pains before birth, reference may be made to the communications by A. Zinsmeister, R. Liertz, C. Long and M. Haarbleicher.

W. Straub states that decomposition of aqueous solutions of scopolamine hydrobromide can be prevented by the addition of mannit. He says that the addition of mannit makes it possible to prepare solutions of scopolamine which are more resistant to the heat required in sterilization and which can be kept for a longer period than those not containing mannit. P. W. Siegel employed solutions of this kind with satisfactory results to produce dawning sleep in his midwifery practice.

To avoid the severe pain produced by injections of alcohol, such as are employed in the treatment of trigeminal neuralgia*, W. Harris suggests injections of hyoscine-morphine in the place of other methods of inducing anæsthesia. Compared with chloroform anæsthesia these injections have the advantage that the patient remains conscious and is able to assist the operator by his statements regarding the position

Hinterstoisser, Wiener klinische Wochenschrift 1913, No. 50, p. 2070.
Zinsmeister, Dissertation Munich 1913.

Liertz, Medizinische Klinik 1913, No. 26, p. 1041.

Long and Haarbleicher, Münchener medizinische Wochenschrift 1913, No. 17, p. 957.

Straub, Münchener medizinische Wochenschrift 1913, No. 41, p. 2279.
Siegel, ibidem 1913, No. 41, p. 2280.

* Compare this Report, p. 79.

Harris, Lancet 1913, I, p. 881.

of the needle. Twenty minutes before making the injection of alcohol the author injected subcutaneously 0.02 gramme ($\frac{1}{3}$ grain) of morphine hydrochloride and 0.0004 gramme ($\frac{1}{150}$ grain) of hyoscine hydrobromide, with the result that the injection of alcohol proved painless. This method of anaesthesia also proved useful in searching for the nerve in the foramen rotundum.

Sedobrol.

Sedobrol*, according to R. Ammann, is a dietetic preparation of bromine which in his opinion fulfils all requirements made of a preparation displaying the maximum of efficacy, apart from the question of freedom from the secondary effects of bromine. Nevertheless, the preparation makes it possible to administer bromine in a practical and convenient form in those cases in which a bromine salt is indicated with a salt-free diet. This view is confirmed by F. Wratschko, F. Deutsch, H. Steffen, von Demole, M. Lauterbach and Engelen.

The use of sedobrol is primarily indicated in epilepsy, as I have already stated in these Reports. Steffen has found it very useful, and in his experience a salt-free diet, which can be enforced for years without harm, in addition to intermittent treatment by bromides, if carefully carried out, yields better results than any other form of anti-epileptic treatment. For the prolonged administration of bromides it is essential to select a palatable form of administration such as is present in sedobrol. With daily doses of 3 to 6 grammes (45 to 90 grains) of bromide it is sufficient to reduce the intake of salt to 8 or 12 grammes (120—180 grains) per diem. To avoid bromism, which can scarcely be avoided with an effective course of bromide treatment, as is apparent from Ammann's statements, Steffen advocates the daily administration

* Compare Merck's Report 1912, p. 394.

Ammann, Deutsche medizinische Wochenschrift 1913, No. 23, p. 1105.

Wratschko, Pharmazeutische Presse 1913, No. 20.

Deutsch, Therapie der Gegenwart 1913, No. 9, p. 394.

Steffen, Wiener klinische Rundschau 1913, No. 13, p. 197.

Demole, Revue médicale de la Suisse romande 1913, No. 5.

Lauterbach, Allgemeine Wiener medizinische Zeitung 1913, No. 26.

Engelen, Deutsche medizinische Wochenschrift 1913, No. 26, p. 1257.

of 1 to 5 grammes (15—75 grains) of sodium chloride and a cautious reduction of the dose of bromide. Bromine acne is treated with arsenic and mercurial ointment, without reducing the dose of bromide. In addition, the author holds that the administration of 0.3 to 1 gramme (5—15 grains) of chloral hydrate, given in the evening, is a valuable adjuvant to the treatment of epilepsy.

Acute and chronic parenchymatous nephritis with and without dropsy afford a further indication for sedobrol. Deutsch, as a rule, prescribed two soups containing 4 grammes (60 grains) of bromide and 0.4 gramme (6 grains) of sodium chloride daily. In addition, the patients were placed on a milk and vegetable diet and allowed an amount of 2 to 5 grammes (30—75 grains) of salt. This medication did not caused diuresis, but in every case it exerted a distinct influence on the excretion of sodium chloride. With these doses bromism never occurred.

Engelen points out that chronic insomnia may be successfully combated by bromine, e. g., sedobrol, if appropriate treatment of the underlying cause is undertaken at the same time. Prolonged bromine treatment is effective, for instance, in migraine and neurasthenic sleeplessness.

Sedobrol consists of sodium bromide, traces of sodium chloride, savoury vegetable extractives and fat. A tablet weighing 2 grammes (30 grains) contains 1.1 to 1.2 gramme (16—18 grains) of sodium bromide and 0.1 gramme ($1\frac{1}{2}$ grains) of sodium chloride. To prepare a broth boiling water is poured over sedobrol, or the preparation is added to soup or food prepared without the addition of salt.

Selenium, Colloidal.

In succession to former reports on the therapeutic use of selenium and its compounds* mention may be made of the more important recent communications on this subject. The use of selenium in the treatment of cancer has awakened considerable interest, and particularly the use of colloidal selenium appears to be gaining in interest. F. Daels undertook a pharmacological and clinical investigation of a preparation of this kind, issued under the name of electroselenium. In rat sarcoma he injected it intravenously and saw that the tumours

* Compare Merck's Report 1911, p. 227 and 1912, p. 180.

Daels, *Geneeskundige Tijdschrift voor België* 1912, Vol. 3, p. 373.

soon exhibited engorgement and became softer, and showed a disposition to break down. In three cases of inoperable carcinoma of the uterus he injected 5 c.c. of electroselenium every second day, and repeated the injection four or five times; after an interval another series of injections were made until twenty injections had been given in all. The injections caused a rise of temperature of 1° to 2° C., the carcinomatous pains were alleviated, the general health improved and they appeared to exert a favourable influence on the bleeding. Bougeant records a similar result; in some cases he even observed a still-stand of the morbid process. He injected 5 to 10 c.c. of electroselenium intravenously every second day, until a total amount of 30 c.c. had been injected. No toxic symptoms or severe disturbance of the general health supervened in any of his sixteen cases, on the contrary, this treatment was as a rule very well borne. On the other hand, M. C. L. Williams failed to obtain a successful result with selenium (seleniol) in mouse carcinoma.

In view of the results recorded in the literature the beneficial action of selenium on carcinoma cannot be denied and therefore is worthy of a more extended trial. A. Braunstein records the results of his investigations. After eosin-selenium* had been found to be too poisonous for human use, the author combined electroselenium with methylene blue and iodine. The value of these three substances has been scientifically established, for colloidal selenium, in common with all the colloids of the heavy metals, stimulates autolytic processes, while methylene blue serves as a carrier, and being also an oxygen-carrier exerts a deleterious influence on the nucleus of the cancer cell. Iodine, as is well known, also has a powerful affinity for cancer cells, in addition to its effect of stimulating autolytic processes. In eighteen cases, some of which were severe, the author injected electroselenium intravenously and at the same time administered 0.1 gramme of methylene blue and 0.36 gramme of iodalbumin per os, in capsules, twice daily. Latterly he prescribed copper-iodine-methylene blue.

Bougeant, Bulletin général de thérapeutique 1912, December.

Williams, Journal of Pathology and Bacteriology 1913, Vol. 17, p. 603.

Braunstein, Berliner klinische Wochenschrift 1913, No. 24, p. 1102.

* Compare Merck's Report 1911, p. 227.

The intravenous injections were well borne by the patients. As a rule, a severe reaction occurred after the first and second injections, consisting in rigor and a rise of temperature up to 39° C. These manifestations passed off after two or three hours, and on the following day the patients usually felt better than before the injections. Several patients did not react at all to the injections. After the third injection the majority of the patients showed no further reaction. In two cases the author saw the occurrence of a rash shortly after the injection, and in three cases intense redness of the face lasting for two or three minutes. He never observed any abnormal symptoms referable to the heart or kidneys, even in a patient who had been given twenty-eight injections. The fact that immediately after the injection several patients stated that they experienced a sensation of pain in the tumour is regarded by the author as characteristic. The effect of selenium-iodine-methylene blue treatment manifested itself in every case by an improvement of the general condition, alleviation or disappearance of the pains, and in several cases a gain in weight became apparent. Objectively subsidence of the ascites, diminution in size and greater mobility of the tumours, and a decrease of the affected lymphatic glands were noted.

N. Trinkler injected electroselenium with successful results in four cases of inoperable malignant neoplasms. He gave eight to eleven subcutaneous, or intramuscular, injections of 5 c. c. each, and in a case of carcinoma of the stomach this treatment led to a remission of the pains and vomiting while the tumour became softer; in a sarcoma of the lip with metastatic lymphatic glands the tumour diminished in size; in a case of carcinoma of the parotid, in addition to a reduction in size of the tumour, the dysphagia and the dyspnoea disappeared; and in a case of peritoneal carcinoma the pains and the ascites disappeared. The injections were well borne when made subcutaneously or intramuscularly into the vicinity of the tumour, but caused pain if made into the tumour itself.

On the other hand, C. Jourdan reports unfavourably on the use of electroselenium. In one case each of carcinoma of the stomach, of the uterus and of the lymphatic glands

Trinkler, Progrès médical 1912, No. 40.

Jourdan, Presse médicale 1912, No. 102, p. 1036.

he gave six intramuscular injections of 5 c. c. each of electro-selenium, one injection every second day, with negative results. R. Philipp also failed to obtain any noteworthy results in a case of sarcoma, carcinoma and lymphosarcoma and had to stop the further use of electro-selenium as rigors, cyanosis, convulsions and other alarming symptoms supervened.

Senna Glucosides.

Whereas A. Tschirch and E. Hiepe ascribe the laxative action of senna leaves to glycosennin, a glucoside insoluble in water discovered by them, R. Tambach states that senna leaves contain two substances with a laxative action, i. e., the "senna glucoside" and "sennoid". The water-soluble glucoside is issued under the name of "sennax". It occurs as a yellowish, amorphous powder, which does not contain any free anthraquinones since it does not give the Bornträger reaction*. In this respect it differs materially from Tschirch's glycosennin. Fehling's solution is not reduced by the senna glucoside in the cold, but is reduced by it on heating. Sennax is supplied in tablets of 0.075 gramme, and in the form of a solution containing 0.075 gramme in one teaspoonful (= 4 c. c.).

S. Schönborn has tried sennax in chronic constipation of the spastic and atonic types, partly complicated with other gastric disturbances, and also in some pronounced neurasthenics. All his cases were severe ones and had persisted for years. He gave one tablet daily (in the evening), up to six tablets every second day. Unwelcome secondary effects such as severe or hæmorrhagic diarrhœas, considerable pain or symptoms of irritation on the part of the uterus, were never observed. The laxative action was as a rule good, although it was insufficient when only one tablet was taken. On the other hand, after taking two tablets it usually set in without fail after eight to ten hours, producing pultaceous stools. The use of two tablets every second day was sufficient to bring about subjective well-being of the patient. However, after

Philipp, Prager medizinische Wochenschrift 1913, No. 34.

Tschirch-Hiepe, Archiv der Pharmazie 1900, p. 427.

Tambach, Pharmazeutische Zentralhalle 1913, No. 27, p. 667.

* Compare Merck's Reagenzien-Verzeichnis 1913, p. 41.

Schönborn, Therapie der Gegenwart 1913, No. 9, p. 392.

the regular use of the drug for some weeks the dose had to be somewhat increased; as an exception habituation to the drug occurred in one patient after a few days.

Sennatin*.

Induced by Credé's favourable reports, Zniniwicz tried sennatin in veterinary practice. He states that it should prove a valuable remedy for colic in horses, at least as far as can be inferred from trials on six horses. In all these cases, in which the intestinal function was almost entirely absent, about three hours after a subcutaneous injection of 20 grammes of sennatin loud intestinal sounds were heard, the intestinal gases were expelled and the animals showed a marked improvement. Defæcation usually occurred three hours later. Should this not occur after six hours the author advises the administration of 0.05 gramme ($\frac{3}{4}$ grain) of arecoline. According to the size of the horse 20 to 25 grammes of sennatin are given. The author did not observe any swelling at the site of injection.

Sera and Antigens.

Anovarthroid Serum.

In discussing the serum therapy of thyroidism R. Hoffmann some years ago pointed out that the serum of sheep from which the ovaries have been removed should prove a promising remedy in the treatment of osteomalacia**. At the time I prepared a serum of this kind for experimental purposes, to which the name of "antimalazin" was given. This preparation was not placed on the market. In view of the fact that the serum of thyroidectomized sheep, known under the name of "antithyroidin Moebius", is also useful in osteomalacia, as Hoffmann was able to demonstrate, the author tried the use of a serum of sheep from which both ovaries and thyroid gland had been removed. For details of the

* Compare Merck's Report 1912, p. 395.

Zniniwicz, Berliner tierärztliche Wochenschrift 1913, No. 19, p. 347.

Hoffmann, Münchener medizinische Wochenschrift 1908, No. 6, p. 279.

** Compare H. Cramer, Münchener medizinische Wochenschrift 1913, No. 15, p. 758.

theoretical bases upon which this treatment rests the original work should be consulted*.

This preparation, to which Hoffmann gave the name of "anovarthroid serum", was used by Klewe-Nebenius in a severe case of osteomalacia. The patient, a woman aged 32, was given subcutaneously nine doses of 10 c. c. each of the serum at intervals of three to five days. The injection was occasionally followed by a slight rash, which disappeared without further disturbances in the course of twenty-four to forty-eight hours. Once transient elevation of temperature to 38° C. occurred, otherwise the injections were well borne. A marked improvement in the course of the disease was seen inasmuch as the patient began to move about without assistance. Her movements were quick and apparently painless, and pressure on the thorax and vertebral column no longer caused pain. Normal menstruation was not restored, and the mental condition remained unchanged. Hoffmann states that further investigations of the action of anovarthroid serum in hyperthyreosis are being undertaken.

Basing on the successful results which have been obtained in the treatment of osteomalacia, Hoffmann holds that the active principles present in his serum are related to the outpourings from the suprarenal glands and the pituitary gland, i. e., adrenalin and hypophysin. Compared with these bodies, which have already been used with successful results in osteomalacia, the serum has the advantage that it contains the secretions of these glands, whereas the others are extracts. It may be administered by mouth in the same way as anti-thyroidin, or subcutaneously in doses of 5 to 10 c. c. at intervals of three to five days.

It is possible that anovarthroid serum may prove useful not only in osteomalacia, but also in rickets, psychoses of puberty, hay fever, otosclerosis, and in vasodilator neuroses in the region of the head (tinnitus).

Antimeristem.

In succession to the communications on this preparation contained in my Reports for 1911 and 1912 mention may

* Münchener medizinische Wochenschrift 1913, No. 13, p. 693.

A reprint will be sent on request.

Klewe-Nebenius, communicated by Hoffmann l. c.

be made of the publications by O. Schmidt, Ritter, V. Gianturco, K. Wagner and M. S. Stockmann. Schmidt reports three cases of cancer, one of carcinoma of the portio, and two of carcinoma of the cervix, in which antimeristem treatment led to a cure. Gianturco also obtained a very gratifying result in a case of scirrhus.

Wagner treated a case of malignant neoplasm, the etiology of which was not definitely established, with antimeristem with the result that liquefaction of the tumour occurred and the patient was relieved of the symptoms. Ritter also believed that he had succeeded in curing a case of carcinoma of the pharynx with antimeristem, but, as he reports later, the patient had a relapse. Stockmann states that antimeristem treatment failed in five cases of cancer. The author holds that the preparation is useless in cases where a surgical operation can afford no relief.

Antithyroidin.

A. Rubino, in an exhaustive work on the results of medicinal and operative treatment of Graves's disease, expresses a very favourable opinion of the action of antithyroidin*. He has prescribed it with marked benefit in mild and severe cases, including cases which had proved refractory to other methods of treatment. He is fully convinced that the preparation is useful in those forms of Graves's disease in which the symptoms, such as irritability, rapid loss of weight, etc., point to the presence of hyperthyroidism, in which it often yields unexpectedly good results. The use of antithyroidin in the treatment of Graves' disease is also fully justified in view of the fact that all observers are agreed that it never causes undesirable secondary effects. However, it is still an open question whether a definite cure may be expected from the use of antithyroidin. With regard to

Schmidt, Zentralblatt für Gynäkologie 1911, No. 51.

Ritter, Meeting of the Berlin Laryngological Society, April 19, 1912.

— Berliner klinische Wochenschrift 1912, No. 24. — Compare

Deutsche medizinische Wochenschrift 1913, No. 20, p. 951.

Gianturco-Marchesini, Medicina nuova 1912, No. 44.

Wagner, Allgemeine medizinische Zentral-Zeitung 1913, No. 48.

Stockmann, Praktischeski Wratsch 1913, No. 11 and 12. — Zentralblatt für Chirurgie 1913, p. 1425.

Rubino, Berliner klinische Wochenschrift 1913, p. 525.

* Compare Merck's Reports 1896—1912 and Merck's Wissenschaftliche Abhandlungen No. 4.

this point Rubino expresses himself as follows: "This is a question to which it is not easy to give a satisfactory reply, because, in contrast to the often long duration of the disease the preparation is administered for a comparatively short time, and there are no means of tracing the cures ascribed to its use. In several instances I have seen a still-stand of the symptoms lasting for years; however, I am not certain that they will not recur, as is so often the case with all kinds of neuroses. Nevertheless, it is beyond doubt that anti-thyroidin yields quicker and more tangible results than can be expected from any other method of internal treatment. Since with all methods of internal treatment it is equally difficult to decide whether a permanent cure has been achieved, it is logical to give the preference to that method which up to the present is known to yield the quickest and most conclusive results".

"With regard to its administration, in my opinion the most suitable method is to give it for a period of twenty days, beginning with a dose of 10 drops and gradually increasing the amount to 100 drops daily, and then to decrease the doses by similar stages; between the first and second series I allowed an interval of four or five days. This series of administrations was repeated as often as was required to obtain the desired result (usually three or four times). Thereupon I still gave the preparation for a further period of twenty days, reducing the doses by one-half, whereupon it was stopped; whenever the symptoms called for renewed treatment it was repeated in the same manner. Of course, in cases in which an energetic action appears indicated the total amount as well as the single doses may be increased; or in cases where the large doses are not tolerated they may be decreased, these cases are, however, far rarer".

The suggestion advanced by some authors that operation should immediately be resorted to in every case as soon as the diagnosis of Graves's disease has been made is opposed by A. Bagrow, W. H. Becker and I. Liebermann. Becker shares Jackson's and Mumford's view that conservative

Bagrow, *Therapeutischeskoee Oboshrenie* 1913, No. 6.

Becker, *Deutsche medizinische Wochenschrift* 1913, p. 1785.

Liebermann, *Minsker Ärztliche Nachrichten* 1913, No. 3.

Jackson, *Boston Medical and Surgical Journal* 1910, Vol. 163, No. 11.

Mumford, *ibidem* 1910, Vol. 162, No. 22.

treatment should be adopted at first, by prescribing rest, strengthening tonics and specific preparations, and if no success is evident to have recourse to operation only when this course is absolutely and urgently indicated. Liebermann records a case in which operation was refused and specific treatment by antithyroidin led to the entire disappearance of all the morbid symptoms, excepting the goitre. The observation that the prolonged use of small doses of antithyroidin often yields surprisingly good results in thyrotoxicosis is confirmed by J. Bauer. This author has also used it with successful results in some patients suffering from pulmonary tuberculosis, and he states that the patients felt better and sometimes gained in weight.

M. Breitmann has also obtained very good results with antithyroidin in the treatment of Graves's disease. He observed, *inter alia*, a beneficial influence on the tremor of the hands, sweating and sleep. Thus, in a case with enlargement of the thyroid, marked drowsiness during the daytime and impaired night rest, under this treatment the drowsiness passed off, sleep during the night was improved and the tremor of the hands disappeared. In addition, the pulse rate fell from 120 to 84 and the subjective discomfort in the region of the goitre diminished, but the sweating was not influenced. In another patient antithyroidin displayed a marked action on fibrillary spasms which had been regarded as an epileptic symptom. Breitmann was able also to confirm the sedative action of the preparation on the heart, already mentioned by other authors. Variations in the action of the preparation in the same patient are ascribed by the author to changes in the condition of the thyroid brought about by alterations in the function of the organ, affections of the genital sphere, the central nervous system, etc. In a case of hysteria which was kept under strict observation and in which hypnosis was quite excluded, he states that the hysterical patient was able to determine exactly when antithyroidin acted and when it failed.

M. Herz reports that antithyroidin proved especially effec-

Bauer, Beihefte zur medizinischen Klinik 1913, No. 5, p. 160.

Breitmann, Therapeutisches Obshrenie 1913, No. 9.

Herz, Wiener medizinische Wochenschrift 1913, No. 22.

tive in the thyrosis which frequently occurs as an accompanying symptom of arterio-sclerosis in aged persons.

In cases of Graves's disease with chronic pancreatitis, starchy dyspepsia and glycosuria without acidosis, Breitmann combined antithyroidin treatment with the administration of pancreatin and taka-diastase and by this means succeeded in obtaining noteworthy successes. Finally he remarks that in some cases of "formes frustes" the action of antithyroidin was so marked as to make it desirable to determine further indications and contra-indications. The author adopted the following dosage: The contents of an original bottle (10 c. c.) are divided into three portions; the first dose is best given during the night. When antithyroidin tablets are used, from the first to third day one tablet is given three or four times daily; from the third to fifth day two tablets are taken three times a day; from the fifth to seventh day two tablets are taken four times daily; from the seventh to ninth day two tablets are given five times a day; after the eleventh day the doses are decreased in the same way until the initial dose is again reached.

A. Schnée also made use of combined treatment with antithyroidin and preparations of the pancreas (pankreon) with gratifying results. He started with the assumption that antithyroidin is capable of displaying a beneficial action only in those cases in which the disease is limited mainly to the thyroid gland, whereas it must fail, entirely or partly, in cases where in addition to the thyroid one or more ductless glands are also affected. The author was able to confirm this assumption experimentally, for in one case of Graves's disease in which marked impairment of the function of the pancreas was manifest, antithyroidin treatment yielded a complete success only when it was combined with the administration of pankreon. In three other mild cases the result of this combined treatment was also satisfactory.

Basing on the results which have hitherto been achieved Georgiewski discusses the relationship of the thyroid gland and diabetes. In succession to the results reported by Lorand and Erben he reports a case of diabetes associated with symptoms of Graves's disease in which antithyroidin

treatment proved successful. The daily administration of 10 c. c. effected a marked improvement of the general condition, and the palpitation and feeling of thirst also disappeared. The author ascribes this result to the effect of the serum of reducing the secretion of the thyroid gland.

Antituberculous Serum.

P. Schrumpf has made a study of Maragliano's antituberculous serum*. After discussing the results which may be expected from the specific treatment of tuberculosis and giving a brief description of the mode of preparation of Maragliano's serum, the author deals with the special indications for, and the use of, the serum. He states that this serum is useful in all cases of uncomplicated tuberculous disease of the lungs, pleura, lymphatic glands, bones, kidneys, bladder and peritoneum, unless they assume from the beginning a rapidly pernicious character. Treatment should be begun at the earliest possible moment and should be continued for a sufficiently prolonged period. The serum is injected either subcutaneously or locally. During the first month of treatment 1 c. c. is injected every second day, whereupon an interval of ten days is allowed; during the second month 1 c. c. and 2 c. c. are injected alternately every second day, and this treatment is continued during the following months, allowing an interval of ten days at the end of each month. The serum may also be given rectally in doses of 2 to 5 c. c., but this mode of administration is not so effective. According to Schrumpf this serum treatment yielded very good results especially in incipient tuberculosis, and he gives some case-histories in support of this assertion. Its administration presents no difficulties and therefore does not call for any special skill, and it is certainly non-injurious.

The use of Marmorek's antituberculous serum is discussed by K. Henius and M. Rosenberg, H. Schlau, Zimmermann, G. Reimann and C. Pavesio.

Schrumpf, *Therapie der Gegenwart* 1913, No. 3, p. 106.

* Compare Merck's *Wissenschaftliche Abhandlungen*, No. 4, p. 78. Henius-Rosenberg, *Deutsche medizinische Wochenschrift* 1913, No. 17 and 18.

Schlau, *Petersburger medizinische Wochenschrift* 1913, No. 11.

Zimmermann, *ibidem* 1913, No. 8.

Reimann, *Beiträge zur klinischen Chirurgie* 1913, Vol. 85, p. 633.

Pavesio, *Riforma Medica* 1913, No. 33 and 34.

Henius reports on the results of clinical treatment with Marmorek's serum. If the patient had not been previously treated by serum he injected it subcutaneously in doses of 5 c. c., until redness and itching occurred at the site of injection, which supervened in the course of from three to fourteen days. Thereupon he proceeded to administer it rectally; after cleansing the bowel 10 c. c. were injected into the rectum, and this treatment was continued daily for months. If the patient had already been given serum, the rectal administration of the serum was immediately resorted to. Out of twenty-three severe cases of pulmonary tuberculosis in which this treatment was adopted, the course of the disease appears to have been beneficially influenced in twelve cases; in six cases the results were doubtful, and in four cases negative. In severe cases which are no longer amenable to active immunization a trial with Marmorek's serum would appear advisable; of course, the use of other effective measures as well should not be neglected.

Rosenberg deals with the use of Marmorek's serum in dispensary treatment. In order not to alarm the patients by the occurrence of anaphylactic phenomena he administered it exclusively by the rectal route. After giving a cleansing enema 20 c. c. of serum were injected rectally, three times weekly, and this treatment was continued, allowing intervals of from two to four weeks every four weeks, until an improvement set in, or until it was evident that this treatment was useless. This treatment never gave rise to any injurious effects, on the contrary, in the majority of cases an improvement in the subjective troubles was noted, and occasionally an objective improvement was seen. Only in six cases of severe pulmonary tuberculosis with cavities no improvement in the condition of the larynx could be demonstrated; however, in three cases the condition of the larynx remained stationary and in two other cases a slight improvement in the condition of the lungs occurred. Two cases of scrofulo-tuberculosis derived no benefit whatever. In the author's experience the most suitable cases for serum treatment are severe cases in the second stage, and mild cases in the third stage. In these cases good results may be expected, whereas in severe cases in the third stage all that can be hoped for is an improvement in the patient's general condition and of the often very distressing subjective troubles. A sine qua non, however, is

that the treatment be continued for weeks or even months. Zimmermann and Schlau also report very good results in severe cases of pulmonary tuberculosis. Reimann's results, too, may be regarded as satisfactory.

Pavesio tried the serum in surgical tuberculosis and especially with its rectal administration saw a marked improvement. He states that local injections in adenitis caused the disappearance of the inflammation.

Behring's Prophylactic Against Diphtheria.

Hitherto diphtheria antitoxin has been used not only as a curative but also as a prophylactic, whereby it has been found that the immunity induced by protective inoculation is of comparatively brief duration (up to a fortnight), while a repetition of the injection of antitoxin excites anaphylactic symptoms owing to the foreign albumin present in the antitoxin. Hence the induction of passive immunity has not always proved entirely effective, in spite of the signal advantages it has rendered in combating diphtheria, especially in epidemics. The results of recent investigations undertaken by von Behring are therefore of the greatest importance since they show that immunity of far longer duration can be produced by active immunization. The new prophylactic is based upon von Behring's observation that diphtheria toxin is not neutralized by antitoxin *in vitro*, and therefore detoxication of the toxin does not take place *in vitro*, as had been hitherto assumed. Therefore, mixtures of toxin and antitoxin in definite proportions may be used to induce active immunization. This observation makes it possible to produce an anthropogenous diphtheria antitoxin for inducing active immunization in the place of the serum obtained from horses. An antitoxin of this kind will probably become superfluous, since Behring's new prophylactic, as its name indicates, is only a prophylactic, and therefore is not intended for use as a curative agent, but for the protective inoculation of persons who are exposed to the risk of infection during an epidemic, e. g., in hospitals, schools, orphanages, families, etc. No definite information can be given at present regarding its method of administration and dosage, as the clinical study of the new prophylactic is not yet concluded. However, it may be stated

that it can be injected subcutaneously, intravenously or intramuscularly, and that it is absolutely harmless, apart from a few local reactions, necessary for a success, such as redness, swelling and painfulness to pressure at the site of injection, or swelling of the regional lymphatic glands. No reference will be made to the dosage, but it may be mentioned that as is the case with tuberculin treatment, treatment is begun with small doses which are increased until the reaction sets in.

Immunity is secured after about three weeks. No definite statement can be made at present regarding its duration, but it may be assumed with a fair degree of certainty that it lasts for years. With regard to the formation of antibodies under the influence of the new prophylactic, in some cases it gave rise to the production of a very high number of units of immunity (up to 600 000 units). Trials have also been made in man with a serum obtained by the active immunization of persons, from which it is apparent that the antitoxin remains unchanged in the organism for a long time. The use of anthropogenous diphtheria serum has a great future before it since the risk of the excitation of anaphylactic symptoms can be obviated. So far reports on Behring's prophylactic against diphtheria have been published by W. Zangemeister, Viereck, Hahn, E. Schreiber, Eckert, Kleinschmidt, Hornemann and Kissling.

Desiccated Serum Ready for Injection (Diphtheria Antitoxin)*.

Compared with liquid sera desiccated sera have the advantage of being far more stable. However, the trouble and

Zangemeister, Deutsche medizinische Wochenschrift 1913, No. 21, p. 977.

Viereck, ibidem 1913, No. 21, p. 978.

Hahn, 30th Congress of Internal Medicine, Wiesbaden, 15—18 April, 1913.

Schreiber, Deutsche medizinische Wochenschrift 1913, No. 20, p. 928.

Eckert, Medizinische Klinik 1913, No. 22, p. 892.

Kleinschmidt, Deutsche medizinische Wochenschrift 1913, No. 41, p. 1977.

Hornemann, Therapeutische Monatshefte 1913, No. 11, p. 757.

Kissling, Deutsche medizinische Wochenschrift 1913, No. 51, p. 2500.

* The desiccated serum ready for injection (German Patent No. 233 693) is prepared in my bacteriological department. It has not yet been placed on the market, but samples for clinical trial will be supplied on request to those interested in this new preparation.

loss of time involved in dissolving them, especially with older preparations, have hitherto stood in the way of their more general employment. Therefore it is interesting to note that W. Eichholz describes a new form of desiccated serum prepared by him which consists of genuine serum free from preservatives, and being absolutely anhydrous cannot undergo bacterial decomposition. For use it is suspended in sterile oil, in which it is protected from the action of the oxygen of the air, so that the preparation retains its efficacy unaltered. Apart from the fact that similarly prepared immune sera, on account of their stability, should prove useful in countries where sera have to be kept in stock for a prolonged period, as is the case in the tropics, there is still another and far more important field of application for desiccated sera. The author succeeded in demonstrating by experiments on animals that the administration of desiccated serum ready for injection does not produce anaphylactic phenomena, since it is absorbed far more slowly from the oily suspension than is the case with liquid sera. Further, animal experiments showed that the curative effect of desiccated diphtheria antitoxin almost equals that of the liquid serum. Hence, unless an immediate effect is desired, there would be no obstacle in the way of the therapeutic use of desiccated diphtheria antitoxin. It is indicated in all cases in which a prompt action is not essential, principally for protective injections, and in cases where serum anaphylaxis is suspected. Eichholz states that in doubtful cases a slightly delayed action (the delay amounting to about one hour) is preferable to exposing the patient to the risks of an anaphylactic shock. However, if there is danger in delay, it is advisable to make an intravenous injection of liquid antitoxin. But if for any reason an intravenous injection is not practicable, an almost equally rapid action can be obtained by the subcutaneous or intramuscular injection of the desiccated serum ready for injection as by the subcutaneous or intramuscular injection of liquid antitoxin.

Dungern's Syphilis Diagnostic.

In order to decide whether Dungern's syphilis reaction*, the technique of which is simpler than that of the Wasser-

Eichholz, Münchener medizinische Wochenschrift 1913, No. 46, p. 2558.

* Compare Merck's Report 1910, p. 340 and 1911, p. 402.

mann reaction and does not necessitate a special laboratory or an intimate knowledge of serological processes, yields sufficiently reliable results in ordinary practice and when applied during the consulting hour, A. Balcarek undertook comparative trials in 101 cases, selected from among the patients of an internal clinic. The results of the author's investigations confirm the value of Dungern's test, for in 96 cases it yielded the same results as the Wassermann test, thus effectively disposing of the doubts expressed by a few investigators regarding the reliability of this simplified modification of the Wassermann test. In three cases it indicated the presence of syphilis, definitely established by the anamnesis, whereas the Wassermann test failed, and only once in a case of hereditary syphilis it gave a positive, and the Wassermann test a negative result. A negative reaction also occurred in a case of cancer of the stomach, in which the Wassermann test gave a moderately pronounced positive reaction.

With regard to the technique of the Dungern test, which is fully described in the directions for use, the author draws attention to a possible source of error which may cast doubt on a positive reaction. This applies to the valuation of the defibrinated blood before applying the test. As is well known, defibrination is effected by stirring the blood with a thin piece of wood. If the sample is taken from a patient whose blood exhibits a lowered time of coagulation, as the author observed in some cases, on account of the small amount of blood used the red blood corpuscles are damaged in a greater degree by the prolonged stirring, with the result that the serum assumes a more or less red coloration. Although with a positive reaction complete agglutination of the red blood corpuscles occurs, nevertheless in these cases the otherwise colourless supernatant fluid is coloured red. In cases of this kind autohæmolysis of the serum may be controlled by transferring the defibrinated blood into small tubes of 3 to 4 mm. diameter in which the blood corpuscles are allowed to settle, until a small meniscus makes it possible to determine the absence of colour of the serum, whereupon the test is carried out. By this means the author avoided any fallacies with positive reactions. In summarizing his results Balcarek comes to the conclusion that the Dungern test fulfils the requirements

made of it. Although the Wassermann test cannot be entirely dispensed with, yet the Dungern test affords a welcome aid to diagnosis for the ship's doctor or the doctor in the tropics who is unprovided with a serological laboratory, or for the small hospital at a distance from the capital.

J. F. von Crippa and Krulle also express a very favourable opinion of the value of the Dungern test. In trials on fifty persons von Crippa found complete agreement between the results of the Dungern and Wassermann tests; he advises adhering to the directions supplied with the outfit issued by Merck. Basing on his experience he considers the method a valuable and serviceable simplification of Wassermann's original method. Nevertheless, where time and circumstances permit its use, the latter should not be dispensed with. On occasionally comparing the results with those of the Wassermann test Krulle always found complete agreement, and he states that the Dungern test even makes it possible to follow the effect of specific treatment. The reaction gradually becomes weaker, i. e., initial non-hæmolysis after some hours is replaced by hæmolysis of constantly increasing degree, until at the end of treatment it takes place in the same way as is the case with non-syphilitic blood. Inversely, after treatment the gradual development of the reaction can also be observed.

In congenital syphilis S. Samelson favours the use of Dungern's modification on the grounds that it is easy of application and has the advantage of requiring only a very small amount of blood. In a case of purulent meningitis the Dungern test proved even superior to the Wassermann test, for the former yielded a negative reaction whereas the latter gave a positive reaction which might easily have led to wrong conclusions.

W. Drügg, K. Wagner and Görl also obtained very satisfactory results by the use of Dungern's diagnostic.

von Crippa, Wiener medizinische Wochenschrift 1912, No. 43.

Krulle, Archiv für Dermatologie, cf. Deutsche Medizinal-Zeitung 1913, No. 11, p. 187.

Samelson, Zeitschrift für Kinderheilkunde 1913, No. 2.

Drügg, Deutsche medizinische Wochenschrift 1913, No. 7.

Wagner, Wiener klinische Wochenschrift 1913, No. 43.

Görl, Münchener medizinische Wochenschrift 1913, No. 22.

Friedmann's Remedy for Tuberculosis.

This new remedy for scrofula and tuberculosis consists, according to F. F. Friedmann, of living, avirulent turtle tubercle bacilli which, even in large doses, are harmless to man and warm-blooded animals, and are obtained by prolonged passage methods and subculture. The preparation is issued in four different ampoules, for four types of injection, viz., 1. intramuscular; 2. simultaneous, i. e., intravenous and intramuscular; 3. intravenous; and 4. intrafistular or intramuscular. The author gives detailed directions for the use of the remedy, and a successful result depends upon the strict adherence to these conditions. As they cannot be briefly abstracted the original paper should be consulted.

As is apparent from the author's communications, and from the statements published by C. L. Schleich, E. Müller, F. Kraus, H. Thalheim, Immelmann and F. Klemperer, the new preparation is a promising remedy for all forms of tuberculosis. H. Lee Barnes' and G. Mannheimer's reports are less favourable.

Pneumococcus Serum.

In succession to St. Saski's experiments, K. E. Boehncke and J. Mouriz-Riesgo undertook an investigation of the various pneumococcus sera principally used in therapeutics, in which these preparations were tested for their content of agglutinins, precipitins, complement-fixing antibodies, bacteriotropins, bactericidins and antibacterial protective substances. Their results may be summarized as follows:

A certain relationship undoubtedly exists between the amount of antibodies contained in a pneumococcus serum and demonstrable in vitro and the degree of protection produced in vivo. This relationship is more marked only in the case

Friedmann, *Berliner klinische Wochenschrift* 1913, No. 44, p. 2070 and No. 45, p. 2082.

Schleich, Müller, Kraus, Thalheim, Immelmann, *Berliner klinische Wochenschrift* 1913, No. 45, p. 2073—2082.

Klemperer, *Therapie der Gegenwart* 1913, No. 12, p. 557.

Barnes, *The Providence Medical Journal* 1913, November. — *Berliner klinische Wochenschrift* 1913, No. 51, p. 2390. Compare also *Therapeutische Monatshefte* 1913, No. 12, p. 888.

Mannheimer, *Berliner klinische Wochenschrift* 1913, No. 28, p. 1301.

Boehncke-Riesgo, *Arbeiten aus dem k. Institut für experimentelle Therapie zu Frankfurt a. M.* 1913, No. 5.

of those antibodies which unquestionably display an action *in vivo*, i. e., the bacteriotropins. An inverse ratio exists in the case of the complement-fixing substances. — None of the sera investigated proved markedly polyvalent, neither *in vitro* nor *in vivo*. However, the author's results show that Merck's pneumococcus serum is undoubtedly polyvalent, but only to a limited extent. — The author was unable to form a definite conclusion regarding the content of complement-fixing antibodies present in the sera. — A study of the keeping properties of the sera showed that the agglutinins are very unstable, whereas the bacteriotropins are relatively stable. After being kept for four to four and a half years experiments to establish their prophylactic effect showed that the sera displayed about a quarter to one-eighth of their original efficacy. From this it may be inferred that no conclusions can be drawn from the content of agglutinins (and of complement-fixing substances?) as to the efficacy of a pneumococcus serum *in vivo*. On the other hand, it is permissible to gauge its efficacy by the content of bacteriotropins demonstrable *in vitro*, from which it follows that a considerable proportion of the specific action displayed by the serum in experiments on animals must be ascribed to the bacteriotropins. Further trials are necessary to elucidate this point.

I have already briefly alluded to the combined use of pneumococcus serum and ethyl hydrocupreine*. The combined use of injections of pneumococcus serum and camphor also appears promising**.

Streptococcus Serum*.**

K. H. Öhmann describes a case of pyo-ovarium which he observed after birth. Since a streptococcal infection was present, and the patient's temperature rose immediately after the operation to 39° C., while the pulse and general condition pointed to the presence of a septic infection, the author injected 20 c. c. of Menzer's streptococcus serum. The serum appeared to exert a beneficial influence, for the temperature

* Compare this Report, p. 221.

** Compare Boehncke, Berliner klinische Wochenschrift 1913, No. 18, p. 820.

*** Compare Merck's Reports 1896—1912 and Merck's Wissenschaftliche Abhandlungen No. 4 (2. Aufl.), p. 66—73.

Öhman, Zentralblatt für Gynäkologie 1913, No. 28.

fell almost immediately to normal, and the woman recovered gradually, so that after three weeks' stay in the clinic she was discharged completely cured.

Welz treated twenty-three cases of erysipelas with Meyer-Ruppel's streptococcus serum. As a rule, he injected 10 c. c. subcutaneously, followed a few hours later by an intravenous injection of 100 c. c. The temperature remained uninfluenced in seven patients, two of whom died; in four patients deferescence occurred by lysis, and in twelve cases the author saw a remarkable conformity in the temperature curves. The intravenous injection was usually followed by a slight rise of temperature, whereupon the fever subsided in the course of the next few hours to rise again moderately on the following day. From the third day the temperature was normal. Coincidentally with the fall in temperature an improvement in the general condition, and frequently in the local process as well, was seen. The injection of serum was occasionally followed by secondary effects which took the form of rigor and a condition resembling collapse, but which only in one case assumed an alarming character. Hence in severe disturbances of circulation care must be exercised in making an intravenous injection, and in individual cases it must be carefully considered whether the severity of the infection warrants this form of treatment.

In the treatment of strangles in horses Rips tried Menzer's streptococcus serum, in addition to other remedies. He gave only one intravenous injection of 50 c. c., which was well borne. A fall of temperature occurred in the three horses in which this treatment was tried, and all were cured.

Tetanus Antitoxin.

K. Kolb and K. Laubenheimer discuss the prophylactic use of tetanus antitoxin, and their work is particularly interesting for the fact that it throws fresh light upon the question whether the injection of antitoxin really has a prophylactic value or not. When antitoxin has been used in wounds which have healed without tetanus supervening it

Welz, *Therapeutische Monatshefte* 1913, No. 4.

Rips, *Zeitschrift für Veterinärkunde* 1913, No. 6.

Kolb-Laubenheimer, *Münchener medizinische Wochenschrift* 1913, No. 9, p. 456.

is difficult to decide, without resorting to a bacteriological examination of the wound, whether healing would have taken place without complications and without infection if antitoxin had not been administered. The authors report the case of a patient who while attending to a threshing machine had sustained a very dirty wound. In the wound *B. phlegmonis emphysematosæ* and *B. tetani* were detected, but after the injection of tetanus antitoxin no tetanic manifestations occurred during the further course of the malady. The absence of tetanic symptoms in spite of the fact that infection had taken place is ascribed by the authors to the abundant use of antitoxin as a prophylactic; nevertheless, they acknowledge that the absence of tetanus may have been due to another possibility. As is the case with other pathogenic germs, it may be assumed that the mere presence of tetanus bacilli on tissues favourable to their development is not in itself sufficient to produce morbid symptoms. In the authors' opinion a definite estimate of the protective action of tetanus antitoxin can only be made if in every case in which it is used the bacterial flora of the wound is ascertained, special attention being paid to the presence of anaërobic germs.

Jacobovici enumerates various precautions which must be observed when using tetanus antitoxin. He states that to avoid toxic symptoms neither a too fresh nor a too old serum should be used. Further, the fact should be taken into account whether the patient has already been treated by antitoxin, since in this case anaphylactic phenomena may occur, and to ascertain whether the serum is well borne not more than 0.25 to 0.5 c.c. should be injected at first. If this amount is tolerated, the full dose is then injected. It is superfluous to add that the antitoxin must be sterile and that local treatment and cleansing of the wound must not be neglected.

F. van der Bogert opposes the widely accepted view that tetanus antitoxin is useless when tetanus has developed. He believes that the failures recorded are solely due to the use of too small doses, and he advocates the use of doses of 150 000 to 220 000 units, which are said to prove extreme-

Jacobovici, *Zentralblatt für Chirurgie* 1913, No. 14, p. 522. — *Spitalul* 1912, No. 15.

Bogert, *Journal of the American Medical Association*, February 1, 1913.

ly useful even in very severe cases. In a case of this kind he injected 587 000 units in the course of three weeks, with the result that the patient recovered.

Sida Rhombifolia L.

During the past year "mesbé"*, a new remedy for tuberculosis, has been tested by a number of investigators. The conclusions drawn by various observers from the results of their investigations may be summarized as follows:

C. Michejda has treated six cases of surgical tuberculosis by mesbé and obtained good results in five cases. He gives no particulars regarding its dosage and method of administration. Butzengeiger also expresses a favourable opinion of the remedy. He employed it in cases of chronic fistulous tuberculosis of the bones, in which the remedy was applied locally in ointment form or on strips of gauze. In one case of costal caries and in another of fistulous tuberculosis of the elbow-joint he obtained a complete cure after ten weeks' treatment, and an almost complete cure in one case of tuberculous disease of the elbow-joint and of the knee-joint respectively. In a case of tuberculous disease of the hip-joint no lasting beneficial influence on the discharge from the sinus could be observed; on the other hand an improvement in the general condition was obtained. In this case about five to six hours after the application of mesbé a reaction occurred, which passed off after about twelve to eighteen hours, and which consisted in pains, elevation of temperature and increased secretion. The author regards this reaction as the proof of a specific action, since it also partly occurred in other cases. However, he is unable to offer any explanation for the action of the drug.

O. Roepke submitted the preparation to an exhaustive test in a large number of cases of pulmonary tuberculosis. He comes to the following conclusions: Mesbé is a new

* Compare Merck's Report 1912, p. 405.

Michejda, Prager medizinische Wochenschrift 1913, No. 9.

Butzengeiger, Münchener medizinische Wochenschrift 1913, No. 3, p. 128.

Roepke, Deutsche medizinische Wochenschrift 1913, No. 4, p. 150.

remedy of unknown composition and mode of action. Its description as a remedy for tuberculosis appears arbitrary. It is certainly no remedy for tuberculosis. Mesbé inhalations and mesbé drink cures fail entirely in pulmonary tuberculosis. The local application of mesbé in tuberculosis of the larynx effects no improvement, far less a cure, indeed it often causes an aggravation of the subjective and objective signs. Therefore mesbé treatment should not be resorted to in sanatoria since it is worthless, and its use for the ambulant treatment of tuberculosis is by no means to be recommended".

H. Klein also comes to the conclusion that mesbé has no specific action in pulmonary tuberculosis. Nor was he able to obtain any results worthy of mention when using it as an adjuvant to the usual treatment. In mild cases it may be given temporarily as a mild expectorant, but its expectorant action is of short duration.

M. Landolt's, Junker's and Jarosch's conclusions are on the whole in agreement with those of the above cited authors.

Silver Arsenite.

O. Rind states that silver arsenite does not, on the whole, display any specific action on any disease, and, in contradistinction to argatoxyl*, he was unable definitely to detect any increase in the number of white blood corpuscles, but he saw that its administration had the effect of stimulating the general vitality of the body. It increases the body's power of resisting disease, and intensifies the action of various drugs, or its administration leads to a display of their full effects. In the author's opinion the field of application of the drug is practically boundless, and this is enhanced by the fact that it is comparatively non-toxic. He has seen surprising results in some cases of acute infectious diseases, for instance, in children with severe intestinal catarrhs and bronchitis, who after the administration of silver arsenite revived and were

Klein, Deutsche medizinische Wochenschrift 1913, No. 33, p. 1594.
Landoldt, Korrespondenzblatt für Schweizer Ärzte 1913, No. 37, p. 1161.

Junker, Therapie der Gegenwart 1913, No. 4, p. 160.

Jarosch, Deutsche medizinische Wochenschrift 1913, No. 5, p. 215.

Rind, Wiener klinische Wochenschrift 1913, No. 25, p. 1028.

* Compare Merck's Report 1911, p. 166.

cured. The author does not give any details regarding the mode of administration and doses of silver arsenite, and only states that it is well borne in large doses, and that one of his patients was given by mouth 3 grammes (45 grains) in the course of six months, without the occurrence of any withdrawal symptoms on stopping the drug. Silver arsenite does not lend itself to injection into the blood stream, at least not in the form in which it was tried by the author, who injected it in 1 p.c. solution, in solution of thiocyanate and thiosulphate, as the injections produced great pain and swellings.

Rind gives no information regarding the chemical composition of silver arsenite, and merely says that, according to the way in which it is prepared, it occurs as a pale yellow or lemon-yellow powder, insoluble in water; it decomposes on exposure to the light. He probably employed a preparation obtained by precipitating silver nitrate with sodium arsenite, but as this method yields preparations of varying basicity and consequently differing in content of arsenic and in their physical properties, and since the dosage is uncertain care should be exercised when using a silver arsenite in testing Rind's statements. Further communications by the author should be awaited*.

Silver, Colloidal (Collargol, Electrargol).

The mode of action of collargol is exhaustively dealt with in a work by K. Gehm. He states that the action of the preparation is principally due to its power of stimulating leucocytosis and to its catalytic properties. The preparation does not display a direct influence on the bacteria which have penetrated into the body, hence its bactericidal action is indirectly induced through the hyperleucocytosis it produces, while the noxious bacterial products are detoxicated and eliminated as a result of its catalytic effect.

K. Weissmann injected colloidal silver intravenously with successful results in a case of bronchiectasis, which had very probably been caused by the aspiration of particles of

* For particulars regarding silver arsenite see C. Reichard, *Berichte der deutschen chemischen Gesellschaft Berlin* 1894, Vol. 27, p. 1022, A. Stavenhagen, *Journal für praktische Chemie* 1895, Vol. 51, p. 1.

Gehm, *Dissertation Munich* 1913.

Weissmann, *Fortschritte der Medizin* 1913, No. 28, p. 757.

food in vomiting during anæsthesia. The patient, a woman, complained of constant cough, foul smelling purulent sputum, vomiting, loss of appetite, lassitude and fever. At first the author administered collargol per os, giving one tablespoonful of a 0.1 p.c. solution of collargol three or four times daily, with the result that the vomiting ceased and the appetite improved. He now proceeded to give intravenous injections of electrargol. He injected each time the contents of an ampoule of 5 c.c., and never observed any rigor, as is said to occur frequently with collargol. The fever abated and coincidentally the sputum decreased and lost its purulent character. The cough likewise was gradually relieved and with it the shortness of breath, while the appetite and sleep improved. The author therefore advocates an energetic treatment by colloidal silver in cases of bronchiectasis and gangrene of the lung.

P. Jelke applied collargol intraperitoneally in diffuse purulent peritonitis. He was induced to adopt this method of application by the well-known beneficial influence of the drug on local suppurative processes and septic conditions. By means of a uterine syringe he injected 30 to 50 c.c. of a 2 p.c. solution, so that it reached all the cavities. However, larger amounts of a more dilute solution may be employed. The author states that the injections can be repeated through the drain, which is an advantage, whereas during operation it is possible to cleanse the abdominal cavity by irrigation only once. The collargol solution is rapidly absorbed from the abdominal cavity without appreciably irritating the peritoneum; it enters into the blood stream by the same path as the infectious material and can therefore immediately display its action. Jelke advocates a further trial of this method.

In those cases of cystitis in which the use of solutions of silver nitrate caused pain J. Trebing prescribed collargol. He directs that the bladder be washed out with a 3 p.c. solution of boric acid and then emptied, whereupon 100 c.c. of a 1 p.c. solution of collargol, warmed to body temperature, are injected by means of a piston syringe and retained as long as possible. The 1 p.c. solution never caused pain, and as long as this does not occur higher concentrations, up to 3 p.c., may be used. The author obtained good results by

this treatment in colicystitis, especially in fresh cases. The fever rapidly abated, the general condition improved, the pains subsided and without exception the urine became sterile. In the presence of high fever the injection should be repeated daily, and after it has abated an injection is made twice or three times a week. The best results were seen in acute gonorrhœal cystitis, in which daily injections caused the disappearance of the manifestations in the course of a week.

According to G. Grund a combination of collargol and quinine is useful in croupous pneumonia. The author gave 0.5 gramme ($7\frac{1}{2}$ grains) of quinine at the latest six to eight hours before the injection of collargol. Occasionally he gave quinine sooner, i. e., 0.5 gramme ($7\frac{1}{2}$ grains) twice daily, and an intravenous injection of 10 c. c. of 1 p. c. collargol solution. Thereupon the administration of quinine was continued for a few days. With this treatment it is possible to effect an immediate fall of temperature leading to a definite recovery, resembling in its manifestations the normal crisis. In other cases the method fails, for reasons which are at present unknown. It does not prevent the occurrence of secondary disease due to localized collections of pneumococci. The author recommends his method in cases where the crisis is abnormally delayed and consequently the malady threatens to run an unfavourable course on account of its long duration. However, even in the early stages a trial holds out a promise of success. Caution is indicated when the heart is extremely weakened.

W. Wolf tried the rectal application of collargol in septic processes, and P. Junghans in articular rheumatism. In a case of sepsis consequent on an operation Wolf injected 25 c. c. of a 2 p. c. solution of collargol, but without result. However, this set in with surprising rapidity after the rectal application of 50 c. c. of a 6 p. c. solution. On continuing this treatment by administering collargol at intervals of a few days the temperature gradually returned permanently to normal. Junghans likewise used collargol with very gratifying results in articular rheumatism. Whereas in about 50 p. c. of the cases the intravenous injection of collargol caused a violent reaction, consisting in rigor, elevation of temperature and disturbance

Grund, Zentralblatt für innere Medizin 1913, No. 47, p. 1169.

Wolf, Deutsche medizinische Wochenschrift 1913, No. 20, p. 944.

Junghans, Deutsche medizinische Wochenschrift 1912, No. 45, p. 2111.

of the general condition, the rectal application of the preparation caused similar, but far milder symptoms. If the heart is quite intact the intravenous route is preferable on account of its prompt action. In these cases 2 c. c. of a 5 p. c. solution are injected. Or 5 c. c. of a 1 p. c. solution may be injected subcutaneously, but this is extremely painful and as regards action has no advantage over the rectal application. For the latter the author used a 5 p. c. solution of which 50 c. c. are slowly injected under slight pressure into the rectum, morning and evening. However, it is absolutely necessary first to clear the bowel of faeces by water enemata, and then of mucous by means of enemata of 1 p. c. solution of soda. The results obtained by this method, coupled with its simplicity, finally induced the author to abandon intravenous injection in favour of rectal application. However, to prove effective, not only must the bowel be cleansed, but the enema should be retained as long as possible in order to permit the absorption of large amounts of collargol.

According to A. Netter, colloidal silver may be used in children's practice; he employed both collargol and electrargol. In bronchopneumonia he recommends inunctions with a 15 p. c. ointment or subcutaneous injections of a solution of 0.25:1000; in severe cases intravenous injections of a 2 to 5 p. c. solution are preferable. These are also useful in rheumatism, infectious endocarditis, pyæmia, and as a substitute for antitoxin in diphtheria. In intestinal diseases of an infectious nature collargol is given internally or rectally; internally in daily doses of 0.02 to 0.04 gramme ($\frac{1}{3}$ — $\frac{2}{3}$ grain), and rectally in doses of 0.4 to 1 gramme (6—15 grains) which are said to yield noteworthy results, especially in typhoid and dysentery. Netter says that too much must not be expected from the injection of the preparation into the pleural cavity, into articular cavities, and into the spinal canal; on the other hand, the local application of a 1 p. c. solution in affections of the nasal cavity exerts a very beneficial effect. Inunctions of collargol are equally promising in erysipelas in infants.

The use of electrargol is reported upon by P. Werner

Netter, *Presse médicale* 1913, No. 3, p. 21.

Werner - Zubrzycki, *Münchener medizinische Wochenschrift* 1913, No. 11, p. 583.

and J. von Zubrzycki, F. Daels, J. Lang, J. Fürth, P. Galli and Schönfeld.

Werner's investigations show that electrargol, in common with all colloidal metals, is capable of increasing in a high degree the opsonic power of the blood serum and thus assists the organism in its fight against pathogenic bacteria. If the hopes which these metals awakened in many instances have not been realized in practice, other factors, according to Werner, than the different virulence of bacteria and the varying power of resistance of the body should be held responsible. In several cases it is not possible to gauge with certainty the beneficial action, or the satisfactory termination of electrargol treatment, for septic processes, for instance, may heal even without treatment by colloidal silver. Daels, who describes seven cases of puerperal sepsis of which only one ended in death, comes to the conclusion that in some of his patients electrargol exerted a beneficial influence on the process. He injected 10 to 35 c.c.

Lang considers electrargol a good adjuvant to operation in septic general infections, especially during after-treatment. However, it is useful only in milder cases, if employed at the earliest possible moment and not stopped too soon after a success is manifest.

Electrargol is deserving of attention in the treatment of gonorrhœal complications, especially in gonorrhœal epididymitis. Fürth injected on an average 5 c.c. into the buttocks three or four times, at intervals of two days, after disinfecting the site of injection with tincture of iodine. In almost all the cases the author saw a rapid subsidence of the often very great pain, and a fall in temperature, whereby the duration of the malady was shortened. As a rule, within a short time the swelling of the epididymis subsided and the tumour decreased in size, but in some cases the hardness due to the remaining infiltration of the epididymis persisted for some time. Electrargol failed entirely only in one case; however, Fürth's case-histories show that on the whole the preparation

Daels, Zentralblatt für Gynäkologie 1913, No.10, p. 329.

Lang, Archiv für Ohrenheilkunde 1913, Vol. 90, No. 4.

Fürth, Dermatologische Wochenschrift 1913, No. 25, p. 689.

Galli, Gazzetta degli ospedali e delle cliniche 1913, No. 14.

Schönfeld, Deutsche medizinische Wochenschrift 1913, No. 30, p. 1461.

exerts a beneficial influence on the course of the affection in gonorrhœal epididymitis.

Galli records three cases of adynamic measles and four cases of hyperpyretic measles. In the former the injection of 5 c.c. of electrargol, repeated three to seven times, brought about a rise of temperature which the author regards as favourable. Two cases were cured. In the hyperpyretic forms of this affection, all of which were cured, the injections apparently had no influence on the temperature, but the author believes that they increased the power of resistance of the body and prevented complications. He states that electrargol treatment also proved useful in measles with complications, since the mortality was lower than formerly.

In severe cases of articular rheumatism recourse may be had with advantage to electrargol, according to Schönfeld, especially when salicylates have proved ineffective. 5 to 10 c.c. of electrargol are given, and this dose can be repeated, if necessary, a few times at intervals of several days. As a rule, the author used a total amount of 10 to 45 grammes of electrargol for a course of treatment.

Two papers by Burchard and Troell are of interest in view of the importance which pyelography has assumed in the röntgenological diagnosis of the kidney. Burchard states that it will reveal the presence of calcification, and will tell whether one healthy kidney is present. On the other hand, in succession to statements by Zachrisson and Jerwell Troell draws attention to the fact that the injection of collargol (for casting shadows) into the renal pelvis is not quite harmless. In one case of doubtful tumour of the kidney Troell injected altogether 6 to 7 c.c. of a 7 p.c. solution of collargol by means of an ureteral catheter, taking care to stop the injection as soon as the patient experienced a feeling of congestion in the region of the kidneys. When the kidney was removed two days later it was found that on the one side collargol had penetrated into the uriniferous tubules and into the renal parenchyma as far as the glomeruli and had set up necrosis and desquamation, and therefore he urges caution when adopting this procedure. On the other hand, W.

Burchard, Fortschritte auf dem Gebiete der Röntgenstrahlen,
Vol. 20, No. 3.

Troell, Hygiea 1913, No. 2.

Schachnow is of opinion that the injection of collargol into the renal pelvis is absolutely harmless if it is properly carried out. He ascribes injurious effects to the use of too high pressure in making the injection, causing a mechanical alteration of the mucous membrane of the renal pelvis, or of the kidney. If this takes place the solution of collargol is able to penetrate into the renal parenchyma where it causes serious damage.

W. I. Bruce gives the following directions for carrying out the injection of collargol: the cystoscope is introduced, the bladder distended with water, and the ureteric catheter passed into the renal pelvis. The bladder is now emptied and the cystoscope is carefully withdrawn, leaving the catheter in situ. A warmed, sterile solution of collargol is allowed to flow in, by the force of gravity only, without exerting any pressure. Any complaint of discomfort or pain in the region of the kidney is an indication to stop the injection, and when this has been decided upon the end of the catheter is plugged and strapped to the patient's thigh. The X ray examination is immediately carried out with the patient lying on his stomach. This method enables some interesting conditions to be discovered, such as double ureters and double pelves, and even tumour of the kidney can be diagnosed by this method. So far this method has been mainly employed for the early diagnosis of hydronephrosis, but in future it may be found to give useful information in other diseases of the kidneys.

Silver Methylene Blue.

A. Edelmann and A. von Müller-Deham undertook a therapeutical investigation of a new preparation of silver in which the silver is combined with methylene blue. The bactericidal action of silver is well known, and in accordance with Ehrlich's and Wassermann's views the methylene blue by acting as a carrier is intended to intensify the action of silver. The new preparation occurs as a blue powder; it contains 20 p. c. of silver and is readily soluble in water. In a solution of 1 in 160,000 it kills various pathogenic bacteria; in the

Schachnow, *Zeitschrift für urologische Chirurgie* 1913, Vol. 2, p. 1.

Bruce, *British Medical Journal* 1913, II., p. 918.

Edelmann-Müller-Deham, *Deutsche medizinische Wochenschrift* 1913, No 47, p. 2292.

blood, where several antiseptics fail, it still displays a sterilizing effect in a dilution of 1:30,000, while in a dilution of 1:80,000 it still checks the growth of bacteria in a marked manner. The preparation is only slightly toxic. Animal experiments showed that given internally it is tolerated in practically any amounts, while subcutaneous doses of 0.1 gramme per kilogramme body-weight are borne without reaction by rabbits.

In general infections the authors gave subcutaneous and intramuscular injections of 0.1 to 0.4 gramme of silver methylene blue (dissolved in 5 to 20 c. c. of water), repeated at intervals of a few days, and found that either mode of application is, as a rule, only slightly or moderately painful. Slight infiltrations at the site of injection quickly subside, and the surgical treatment of a sterile abscess is rarely required. The dye is in great part eliminated with the urine, but never by the skin, so that staining of the skin need not be feared. No secondary effects referable to the central nervous system, digestive organs, circulation or kidneys were observed.

The authors gained the impression that injections of silver methylene blue exert a beneficial influence on the course of the malady in septic processes. Although a definite influence on the temperature could not be established in every case, nevertheless the virulence of the infection was apparently weakened by this treatment, and an improvement in the general condition always set in. Two cases which ended in death owing to complications formed an exception; on the other hand nine cases were cured.

In acute articular rheumatism the preparation proved effective in cases in which salicylates and atophan had failed. At first the pains and swellings subsided, then the fever fell by lysis. Complications such as endocarditis and pericarditis also disappeared. Tuberculosis, lymphogranulomatosis and croupous pneumonia do not appear to be appreciably influenced, but in one case post-pneumonic fever of long-standing was quickly cured. Likewise in a severe case of pyelitis the fever disappeared and the appearance of the urine improved. Of two cases of colitis one was cured by local treatment while the other was only moderately influenced. The authors tried the local application of the preparation in gonorrhœa and furunculosis; in furunculosis they injected small amounts

into the furuncles and obtained by this means a surprisingly rapid cure.

In gonorrhœa, too, the preparation displayed an energetic action. The authors intend publishing the results obtained by silver methylene blue treatment in this indication, and also in suppurating bubo, and their paper will doubtless give full particulars concerning the doses and indications.

J. Saphier and L. von Zumbusch maintain that the silver methylene blue treatment of buboes is considerably more effective than the usual method. They treated 124 cases and came to the following conclusions: 10 p. c. of the cases healed in two days, i. e., on changing the dressing for the first time it was found that the puncture wound was closed, the inflammatory redness and the painfulness had disappeared, and on aspirating or pressing no fluid escaped. No relapse occurred during the further period of observation. 20 p. c. of the cases required three to five days; 30 p. c. six to eight days; and 35 p. c. about a fortnight. In 5 p. c. of the cases the buboes did not become "chancrous". However, even in these cases, in which the prognosis was bad from the beginning the use of silver methylene blue yielded better results than the customary method of treatment. On the other hand, so-called strumous buboes were but little influenced by the preparation.

The treatment is carried out as follows. The affected area is cleansed with benzin and after disinfecting with tincture of iodine a puncture is made in the centre of the suppurating bubo; the puncture should not be larger than the nozzle of a Record syringe. After aspirating or expressing the pus solution of silver methylene blue is injected in excess into the emptied cavity. Thereupon a moist compress is applied and allowed to remain in situ for at least 48 hours. The authors employed a solution containing from 0.5 to 5 p. c. of silver methylene blue. The solutions never caused pain, and proved more effective than a 1 p. c. solution of silver nitrate, a 1 p. c. solution of sodium chloride, or a 5 or 10 p. c. solution of protargol. Basing on the results of their investigations the authors consider silver methylene blue the best preparation for the treatment of suppurating buboes.

Silver Nitrate.

O. Wulff reports on Rovsing's method of treating burns, which is carried out as follows:

First of all the healthy skin surrounding the wound is cleansed with soap, water and alcoholic solution of mercuric chloride, and after opening any blisters which may be present the burns are carefully cleansed with soap, alcohol and carbolic acid lotion. This very painful manipulation is, under circumstances, best carried out under ether anaesthesia. After the wounds have been cleansed they are covered with sterile guttapercha tissue in which several small incisions have been made, care being taken to ensure that it extends 0.5 cm. beyond the margins of the wound. Over the guttapercha tissue a thick layer of 1 p.c. silver nitrate gauze is laid and the whole is covered with sterile cotton wool, whereupon the dressing is fixed by means of a gauze bandage. If necessary this treatment is assisted by the administration of narcotics, stimulants and infusions of salt water.

Compared with the direct application of a dressing to the burns this method has the advantage that the dressing does not stick to the wound and does not cause pain when it is changed. Further, the newly formed epidermis is protected, the granulations are not injured and the healing process runs a smoother course. At the same time the guttapercha tissue has a cooling effect on the wound, in the same way as oil and similar remedies. Suppuration is limited to a minimum, necrotic débris are quickly thrown off and the wound is gradually covered by epidermis, beginning from the margins. In burns of the first degree and in slight burns of the second degree healing is said to take place within a surprisingly short time. In larger wounds, or where there is more suppuration, on changing the dressing the wounds should be irrigated with salt water to stimulate epithelialization; boric acid powder may be dusted on the granulating surfaces. The discharge from the wound passes through the holes in the guttapercha tissue and is absorbed by the silver nitrate gauze, which displays a continuous antiseptic action and prevents increased suppuration. This treatment also prevents the occurrence of the much feared contractions, at least these did not supervene in any of the sixty cases treated by the author.

G. Weidenbaum deprecates the use of solution of silver, on account of its irritant effect, for the prophylaxis of ophthalmia neonatorum, and recommends the use of a freshly prepared solution of silver nitrate in the place of the newer preparations of silver and albumin, solutions of which are difficult to prepare and do not keep. At his suggestion I now supply tablets of silver nitrate which can be conveniently carried in the midwifery bag. In their preparation potassium nitrate is used as the excipient, for the author's investigations showed that it does not irritate the cornea when applied either in substance or in solution. Each tablet contains 0.1 gramme ($1\frac{1}{2}$ grains) of silver nitrate and 0.1 gramme ($1\frac{1}{2}$ grains) of potassium nitrate, and is readily soluble in water at ordinary temperature. By dissolving one tablet in 10 c.c. of water a 1 p.c. solution is obtained. For this reason these tablets are also useful in midwifery.

Ochsenius states that painting with a 2 p.c. solution of silver nitrate offers a specific method of treating whooping cough. His procedure is simple and conservative, but a complete success can only be obtained if it is adopted at the earliest possible moment, i. e., as long as the infection is limited to the upper air passages. In these cases a cure can be effected within a few weeks without a change of air. The treatment consists in thoroughly painting the throat of the child every second day during the first two weeks, whereupon a few days are allowed to elapse in order to observe the effect. As a rule, a sudden change occurs at the end of the second, or during the third week of treatment. If the number of attacks is not reduced, or even increases, the painting is continued for another week. In infants the author advises daily painting in the beginning. It may be mentioned that an increase in the number of attacks is frequently seen on the day following the painting.

H. Albert recommends painting with a solution of silver nitrate for the treatment of diphtheria carriers. He obtained the best results by the treatment of the crypts of the tonsils with a 5 to 10 p.c. solution, applied by means of a cotton-

Weidenbaum, *Petersburger medizinische Wochenschrift* 1913, No. 11, p. 134.

Ochsenius, *Therapie der Gegenwart* 1913, No. 11, p. 502. — *Semaine médicale* 1913, No. 48, p. 569.

Albert, *Journal of the American Medical Association*, September 27, 1913.

wrapped flexible applicator. This treatment is combined with a mild alkaline and antiseptic spray for the nasal cavity, and a 1 p.c. solution of hydrogen peroxide as a mouth wash and gargle.

Simaruba Officinalis D C.

In a paper on the treatment of dysentery K. Justi draws attention, *inter alia*, to the fact that the root-bark of *Simaruba officinalis* is a good antidysenteric, which has the advantage over *ipecacuanha* of not causing vomiting. As far as I am aware, *simaruba* has long been known as a remedy for dysentery, and was probably already used by the natives of Cayenne and West India for this purpose; however, no recent confirmation of the curative value of the drug in amœbic dysentery has come to my knowledge. In amœbic dysentery Justi made use of the following prescription which, in addition to *simaruba*, also contains other amœbicides:

Rp. <i>Simarubæ</i> pulv.	3 grammes (45 grains)
Benzonaphthol.	3 „ (45 „)
Bism. subnitr.	8 „ (120 „)
Syr. Kramer.	30 „ ($\frac{2}{3}$ oz)
Syr. <i>Acaciæ</i> (Senegal)	200 „ (5 oz)

M. Sig.: 1 tablespoonful every 3 or 4 hours.

Another prescription known in Hong Kong under the name of "Dr. Rhein's remedy", according to Justi reads as follows:

Rp. Rad. <i>Simarubæ</i>	1750 grammes (62 oz)
Cort. <i>Cinnamomi</i>	875.5 grammes (31 oz)

Three litres ($5\frac{1}{4}$ pints) of water are added to the mixture, which is boiled down to two litres ($3\frac{1}{2}$ pints), whereupon three tablespoonfuls of brandy are added. After thorough cleansing of the bowel by means of castor oil a wineglassful is given four times daily.

Sodium Bicarbonate.

The use of sodium bicarbonate* in diabetes and acetonuria is discussed by F. Rolly, R. Novoa, P. Ohnacker and Magnus-Levy.

Justi, *Münchener medizinische Wochenschrift* 1913, No. 14, p. 765.

* Compare Merck's Report 1912, p. 411.

Rolly, *Medizinische Klinik* 1913, No. 15, p. 568.

Novoa, *Gaceta medica Catalana* 1912, p. 242.

Ohnacker, *Dissertation Giessen* 1913.

Magnus-Levy, *Münchener medizinische Wochenschrift* 1913, No. 47, p. 2650.

Rolly is of opinion that once coma has supervened nothing can be done, therefore the occurrence of coma should be prevented as far as possible. For this purpose, in addition to appropriate diet, sodium bicarbonate is given in increasing doses until the urine becomes alkaline. Thereupon the doses are slightly reduced until the urine is once more faintly acid. In this way 5 to 50 grammes (75—750 grains) of sodium bicarbonate can be administered daily in the beginning. Under this treatment the excretion of acetone bodies in the urine is increased, i. e., the elimination of toxic substances is promoted. For this reason alone sodium bicarbonate should be given in severe cases of diabetes, even if one does not incline to regard diabetic coma as being due to poisoning by acid. It also follows that the administration of sodium bicarbonate favours the formation of acetone substances in the body, as is apparent from Novoa's investigations, with this difference that under the influence of this medication the amount excreted is greater than the amount formed, so that in every case a therapeutic effect is obtained. This is borne out by the experience that by the use of sodium bicarbonate the onset of coma can at least be delayed for a considerable time. If in spite of this treatment coma occurs, one litre of a 3 to 5 p.c. solution of soda should be slowly injected intravenously. At the same time large amounts of sodium bicarbonate are given by mouth and 50 grammes of solution of soda are injected into the rectum several times daily. Diuretics are also given as adjuvants. The author has likewise obtained gratifying results with infusions of physiological salt solution, a method which has recently been advocated by some writers*. The latter are given for the purpose of diluting the poison present in the body, which is then eliminated by the kidneys. Three to five litres of physiological salt solution, sometimes combined with solution of soda, are infused daily.

Ohnacker advocates the administration of very large doses of sodium bicarbonate (up to 240 grammes [$8\frac{1}{2}$ oz]) daily, since he believes that a very large amount of acid has to be neutralised. In his opinion it is best given by mouth. However, the administration of sodium bicarbonate must be begun as soon as

* Compare Achard and Ribot, *Semaine médicale* 1913, No. 10, p. 117. — *Presse médicale* 1913, No. 19, p. 181 and No. 21, p. 2001.

possible and should not be stopped too soon after the subsidence of the symptoms of coma.

Magnus-Levy controverts the view that subcutaneous injections of sodium bicarbonate cause necrosis. The latter effect is due to the fact that during sterilisation of the solution sodium bicarbonate is partly converted into sodium carbonate; if the amount of carbonic acid lost in this way is replaced, a 4 p.c. solution can be injected subcutaneously without harm. These injections are only required in coma, in the absence of another method of application.

Sodium Cinnamate (Hetol).

P. Cohn, who already reported on the value of hetol in keratitis parenchymatosa several years ago*, places on record the results of further trials with this drug** in eye work. He deals with the treatment of tuberculous iritis, in which, according to Groenouw's statistics, so far few successes have been achieved. Instillations of hetol yielded such excellent results that the author's method of treatment by hetol deserves wider recognition, all the more so since it is very simple. A 2 to 5 p.c. solution of sodium cinnamate is instilled into the conjunctival sac every second day, and the number of drops is increased during the course of the treatment. To render the application painless 1 p.c. of novocaine is added to the solution of hetol, and before applying the latter one drop of a 3 p.c. solution of cocaine is instilled.

Sodium Mercurio-Nucleinate.

J. Almkvist reports on the use of sodium mercurio-nucleinate in the treatment of secondary syphilis. He employed a preparation containing 10.21 p.c. of mercury attached to nitrogen, hence it yielded no precipitate of mercury, either as sulphide with hydrogen sulphide, or as metal with copper. He gave intramuscular injections of a 10 p.c. aqueous solution of the preparation, in single doses of 0.5 to 1 c.c., the equivalent of 0.05 to 0.1 gramme of sodium mercurio-nucleinate, or of about 0.005 to 0.01 gramme of mercury. Apart from the injections no local treatment was undertaken.

Cohn, Münchener medizinische Wochenschrift 1913, No. 18, p. 979.

* Merck's Report 1906, p. 230.

** For reports on hetol see Merck's Reports 1898—1909.

Almkvist, Dermatologische Wochenschrift 1913, No. 39, p. 1147.

The cases described by the author show that sodium mercurio-nucleinate displays a comparatively powerful action on various symptoms of secondary syphilis. Thus, well marked roseola eruption disappeared after from six to sixteen days' treatment, fully developed mucous papules of the vulva and anus disappeared completely, within nine to twenty-two days; hypertrophic mucous papules disappeared after thirty days; ser-piginous papules on the penis and scrotum after twelve days; and annular papules on the neck after ten days. In two out of five cases the Wassermann reaction was influenced. Symptoms of mercurial intoxication, colitis, stomatitis, or albuminuria never occurred. On the other hand, the preparation gave rise to local as well as general reactions which may assume such intensity as to become unbearable, therefore its use in general practice is likely to be fraught with difficulties.

Sodium Nucleinate.

As I have already reported elsewhere*, a combination of sodium nucleinate and mercury can be employed with advantage in the treatment of syphilis. This also holds good for the treatment of metasymphilitic processes such as paralytic dementia, to which attention has already been drawn by J. Donath. In a recent work Donath states that when antisymphilitic treatment is indicated preference should be given to a combination of sodium nucleinate and salvarsan. If the case calls for prompt treatment, the author advises at first the use of salvarsan, followed by sodium nucleinate. For this purpose a 10 p. c. solution of sodium nucleinate is used, to which 1 p. c. of sodium chloride is added. As an initial dose 1 gramme (15 grains), in some cases 0.5 gramme ($7\frac{1}{2}$ grains), of sodium nucleinate is given, and, if necessary, the dose is gradually increased by 0.5 to 1 gramme ($7\frac{1}{2}$ —15 grains) until 4 or 5 grammes (60—75 grains) are injected, in order to produce a sufficient amount of lymphocytosis and elevation of temperature. The temperature may rise to 38.5°C ., or even to 40.5°C ., and the leucocyte count to 15 000—23 000 or even higher. The injections are given at intervals of five days.

Other investigators besides Donath have also obtained good results by treatment with sodium nucleinate, as I have

* Compare p. 21.

Donath, *Münchener medizinische Wochenschrift* 1912, No. 42 and 43.

Donath, *Therapie der Gegenwart* 1913, No. 11.

already stated. In tabes and paralysis, and in all syphilitic affections of the central nervous system Donath begins with an intravenous injection of 0.3 gramme of neosalvarsan, and increases the dose at intervals of five to seven days up to 0.45—0.6 gramme, in robust patients up to 0.75 gramme. In weakly persons he repeats the dose of 0.6 gramme. In very robust individuals treatment may be begun with a dose of 0.45 gramme. In the intervals intragluteal injections of enesol are made at intervals of two days. After giving twenty to thirty injections of enesol three infusions of neosalvarsan may still be made, beginning with 0.45 gramme.

Sparteine Sulphate.

Wolferton speaks highly of the value of sparteine as a cardiac tonic. His investigations show that it is the most reliable cardiac stimulant, and often proves superior to digitalis, if it is given in appropriate doses. He states that sparteine is at least as effective as digitalis. It is very useful in high intra-arterial vascular pressure, which is a contra-indication to digitalis. To this must be added the advantage that sparteine is free from the unwelcome secondary effects of digitalis, such as cumulative action and irritation of the stomach. In contradistinction to Frommüller and Stössel, and in agreement with Kurloff, Wolferton lays stress upon the reliable diuretic effect of sparteine which, he states, soon manifests itself. Sparteine is practically indispensable in anuria and oliguria, and is likewise useful, as a curative and prophylactic, after operations. To obtain a satisfactory effect 0.06 to 0.12 gramme (1 to 2 grains) of sparteine sulphate are administered by mouth every two to six hours; if necessary, it can be injected subcutaneously, in doses of 0.1 gramme (1½ grains), at first every two hours and later at longer intervals (four to six hours).

Strophanthidin.

F. Feist already demonstrated that on heating k-strophanthin with hydrochloric acid it is split up into strophan-

Wolferton, *Therapeutic Gazette* 1913, May.

Frommüller-Stössel, *Merck's Report* 1911, p. 112.

Kurloff, *Merck's Report* 1911, p. 113.

Feist, *Berichte der deutschen chemischen Gesellschaft Berlin* 1898, Vol. 31, p. 538; 1900, Vol. 33, p. 2063 and 2069, and 2091.

thidin (k-strophanthidin) and strophanthobiose-methyl ether. Strophanthidin forms white crystals, soluble in alcohol and insoluble in water, which melt at 169° — 170° C., of the chemical formula $C_{27}H_{38}O_7, 2H_2O$.

So far strophanthidin has awakened no interest in therapeutics, probably because it has been assumed that it is devoid of any action on the heart, in analogy with the cleavage products of digitalis. That it is poisonous was already demonstrated by Fraser by experiments on frogs. Pharmacological tests recently undertaken by A. Gröber show that strophanthidin displays a typical digitalis action on the heart. On the other hand, E. Hessel found that g-strophanthin is only with difficulty completely broken up by acid, and further that strophanthidin which is absolutely free from strophanthin has no action on cold-blooded and warm-blooded animals.

Strophanthin.

The excellent action of k-strophanthin in acute cardiac weakness, frequently mentioned in my Reports*, has been fully confirmed by the results of O. Thorspecken's investigations. He found intravenous injections of strophanthin to be a sovereign remedy in the treatment of chronic cardiac weakness, when the galenical preparations of digitalis are not tolerated. When giving strophanthin care must be taken to assure oneself that the patient is no longer under the influence of digitalis. After a sufficiently long time has been allowed to elapse after the last dose of digitalis, 0.5 milligramme of strophanthin is tentatively injected intravenously, and twenty-four hours are allowed to elapse before repeating this dose; if necessary, the dose may then be increased to 0.75 milligramme. If 1 milligramme has been injected at least thirty-six hours must elapse before giving another injection. This treatment is especially indicated and is of value in engorged liver and in contracted kidney.

Fraser, Transactions of the Royal Society of Edinburgh Vol. 35, IV. p. 955 and Vol. 36, II. p. 343.

Gröber, Archiv für experimentelle Pathologie 1913, Vol. 72, p. 317.
Hessel, Sitzungsberichte der naturforschenden Gesellschaft zu Rostock 1913, Vol. 5; Chemiker-Zeitung 1913, Repert. p. 567.

* Compare Merck's Report 1911, p. 116 and 1912, p. 432.

Thorspecken, Deutsches Archiv für klinische Medizin Vol. 110, No. 3 and 4.

Of purely physiological, or pharmacological, interest are the works on strophanthin by A. Bickel and M. Pawlow, V. Weizsäcker, O. Gros, C. J. Rothberger and H. Winterberg, A. J. Clark, Berti and Malesani. As these do lend themselves to brief abstraction the originals should be consulted.

Strychnine.

Whereas of late greater caution has been observed with regard to the dosage of strychnine and its maximum doses have been reduced*, quite recently the view has been advanced that large doses exert a marked tonic effect. Thus P. Hartenberg has given large doses of strychnine in the form of subcutaneous injections for over ten years with good results, and he has found strychnine to be an excellent nerve tonic. It is a specific "muscle food" and in muscular atrophy and muscular atony its use deserves wider recognition than has hitherto been the case. However, in order to obtain satisfactory results it must be given in large doses, subcutaneously, and for this purpose strychnine sulphate should be prescribed, which the author considers more effective than the other salts of strychnine. To enable the introduction of large doses the organism must be habituated to the poison and this is achieved by gradually increasing the doses. It is advisable to employ a solution containing 1 gramme of strychnine sulphate in 100 c. c. of water, of which 1 c. c. contains 0.01 gramme of strychnine sulphate. The solution must be carefully filtered and sterilized and protected from impurities. It is best put up in ampoules of 1 c. c., and after opening an ampoule and withdrawing the amount required the remainder should be poured away. Further, a Pravaz syringe is used every division of which

Bickel-Pawlow, *Biochemische Zeitschrift* 1913, Vol. 48, p. 459.

Weizsäcker, *Archiv für experimentelle Pathologie* 1913, Vol. 72, p. 282.

Gros, *ibidem* 1913, Vol. 71, p. 364.

Rothberger-Winterberg, *Pflügers Archiv für die gesamte Physiologie* 1913, Vol. 150, p. 217.

Clark, *British Medical Journal* 1913, II. p. 897.

Berti-Malesani, *Archives italiennes de biologie* Vol. 54, p. 917.

— *Nouveaux remèdes* 1913, No. 20, p. 466.

* In the last edition of the German pharmacopœia the maximum doses of strychnine were reduced by one-half.

Hartenberg, *Presse médicale* 1913, No. 8, p. 71.

corresponds to one drop of the solution, i. e., the equivalent of 0.0005 gramme of strychnine sulphate. For women the initial dose is four divisions (= 0.002 gramme), and for men eight divisions (= 0.004 gramme); this is a dose which does not produce any reactions such as dizziness, slight feeling of intoxication, rigidity of the jaws and legs. However, to obtain the maximum of effect this reaction must be produced, therefore the doses are gradually increased. This reaction usually occurs in women after injections of 0.005 to 0.006 gramme of strychnine sulphate, and in men after injecting 0.006 to 0.007 gramme. But even when the reaction has set in the dose should still be cautiously increased, since the organism is beginning to become habituated to the strychnine and larger doses are required to produce the reaction. If, in spite of increasing the dose by half a division, the reaction should occasionally prove too violent treatment is continued without altering the dose. In intelligent patients who are, to a certain extent, able to control the course of treatment, it is possible to reach a daily dose of 0.01 to 0.02 gramme, or several doses of 0.01 gramme each, without having to fear a cumulative action. The elimination of strychnine appears even to increase with the increasing doses and is accomplished in about three to four hours. With this method Hartenberg has achieved very good results in neurasthenia, medullary and neuritic affections, muscular atrophy, cachexia, etc.

Troisfontaines came to similar results, and in case of emergency he advises that the injection of 0.01 gramme of strychnine should be repeated every four or five hours. He prefers the use of strychnine nitrate. In chronic cases he injects daily 0.01 gramme during the first four days of treatment, and then increases the dose by 0.005 gramme on the following days, so that after ten days a daily dose of 0.025 to 0.03 gramme is reached. This dose can then be given for months without apprehension. In alcoholics the daily dose may even be increased to 0.05 gramme of strychnine nitrate.

The effect of strychnine in sciatica described by M. Retiowow is doubtless based upon its tonic action. Subcutaneous injections of 0.002 gramme of strychnine nitrate are said to act all the more promptly the more acute the symptoms. Ac-

cording to A. Taddei they yield excellent results in retention of urine in paralytics.

Reference can only be made to the physiological, or pharmacological, works by W. Heubner, S. Loewe, G. Bickeles, L. Zbyzewski and A. A. Tetjeff.

Stypticin*.

A. Sigrist has published a paper on the treatment of profuse hæmorrhage consequent on extraction of teeth and operations on the dental pulp. He reports a case of hæmophilia in which the styptic action of stypticin was displayed in a typical manner. After the extraction of a lower molar in a boy profuse hæmorrhage occurred which could not be arrested by iron perchloride nor by the cautery or the application of 10 p.c. iodoform gauze. Therefore a plug of stypticin gauze was inserted into the alveolus, and at the same time a 5 p.c. solution of stypticin was injected subcutaneously into the cheek and tongue. A further injection made into the arm effectually checked the hæmorrhage.

Stypticin likewise yields excellent results in the troublesome bleeding in extirpation of the pulp. In cases of this kind the author refrains from cauterising the pulp on account of the deep action of arsenic, and instead anæsthetises it. As soon as the excavator reaches the vicinity of the roof of the cavity and a horn of the pulp has been exposed, he places a few crystals of stypticin on the exposed pulp, seals the tooth for ten minutes with cotton wool and mastic, and then completely exposes the cavity. After removing the pulp the following paste is introduced:

Rp. Zinc. oxid. .	2 grammes (30 grains)
Thymol. pulv.	0.2 gramme (3 grains)
Stypticin.	0.2 gramme (3 grains)
Glycerin. q. s. ut f. pasta.	

On capping the extirpated pulp with this paste in fifty cases the author never saw any bleeding.

Taddei, *Semaine médicale* 1913, No. 6, p. 67.

Heubner-Loewe, *Archiv für experimentelle Pathologie* 1913, Vol. 71, p. 174.

Bickeles, Zbyzewski, *Zentralblatt für Physiologie* 1913, Vol. 27, p. 433.

Tetjeff, *Dissertation St. Petersburg* 1913. — *Zentralblatt für die gesamte innere Medizin* 1913, Vol. 7, p. 206.

* Compare Merck's Reports 1895—1912.

Sigrist, *Zahnärztliche Rundschau* 1913, No. 16.

Styracol.

In the treatment of tuberculosis A. Mühsam¹ has tried a combination of styracol* and tuberculin in hospital and out-door patients. They were mostly patients who attended to their occupations and came to the consulting-room for treatment. Basing on eighteen case-histories the author comes to the conclusion that styracol is a valuable adjuvant to the treatment of pulmonary tuberculosis. Given in tablets the preparation is readily taken; it is best administered after meals**. Eructation and a taste of creosot which are at first experienced are soon overcome. Shortly after beginning the regular use of styracol tablets the appetite shows a decided improvement, and in view of the absence of appetite in tuberculotics this effect is highly desirable. At the same time the expectoration becomes more mucoid and the quantity diminishes. In one case this effect was obtained by the use of styracol alone, without resorting to any other measures.

Sugar in Blood, Estimation of, According to Kowarsky's Method.

For clinical purposes it is often of importance to ascertain the sugar content of the blood of a diabetic, for instance prior to operative procedures. For the examination of blood by the methods so far available a large amount of blood (10 to 20 c.c.) was required, until Bertrand described a new method which consists principally in boiling the blood or blood serum with an alkaline solution of copper sulphate, and, after washing the cuprous oxide which is precipitated, it is dissolved in solution of ferric sulphate, and the amount of iron which is reduced is titrated with solution of potassium permanganate. Since this method does not yield accurate results if very small amounts of sugar are present in the blood, it was modified by A. Kowarsky, who adds a known amount of glucose to the sample of blood with a

Mühsam, Therapie der Gegenwart 1913, No. 10, p. 478.

* Compare Merck's Report 1908, p. 330.

** The dose for adults is 1 gramme (15 grains) = 2 tablets, 3 or 4 times daily.

Bertrand, Bulletin de la société chimique de France 1906, Vol. 35, p. 1285. — Merck's Reagenzien-Verzeichnis 1913, p. 30. —

Comp. Sonntag, Biochemische Zeitschrift 1913, Vol. 53, p. 501.

Kowarsky, Deutsche medizinische Wochenschrift 1913, No. 34, p. 1636.

very low content of sugar; the amount of glucose added is then deducted when calculating the result. To apply this test the following reagents are required:

Solution I. 8 grammes of pure copper sulphate and 0.1 gramme of chemically pure glucose are dissolved in water and sufficient water is added to make 200 grammes.

Solution II. 40 grammes of sodium potassium tartrate and 30 grammes of sodium hydroxide are dissolved in water to 200 grammes.

Solution III. 10 grammes of ferric sulphate are dissolved in 40 c.c. of concentrated sulphuric acid and sufficient water is added to make 200 grammes.

Solution IV. A solution of 1 gramme of potassium permanganate in 200 grammes of water which must be always freshly prepared before use; it is diluted with ten times its volume of water before use. To standardise this dilution a solution of 0.1 gramme of ammonium oxalate in 100 c.c. of water is prepared, 10 c.c. of which, after the addition of 2 c.c. of sulphuric acid, are titrated until a permanent pink tint is produced. The constant index 8.95 is divided by the number of cubic centimetres of the solution of potassium permanganate used, and the resulting figure indicates the number of milligrammes of copper corresponding to 1 c.c. of the solution of potassium permanganate. If, for instance, 9.8 c.c. of KMnO_4 solution have been used in titrating, then 1 c.c. of the solution of potassium permanganate corresponds to $= 8.95 : 9.8 = 0.91$ milligramme of copper.

In addition to the above solutions liquor ferri oxydati (Merck), which is diluted with equal parts of water, powdered sodium potassium tartrate and a 2 p.c. solution of sodium fluoride are required. The distilled water should be free from organic impurities, therefore it is advisable to employ freshly distilled water*.

Briefly, the procedure is as follows: The finger-pad is cleansed with alcohol and a deep puncture is made so that large drops of blood are shed without pressure. 0.5 c.c. of blood is added to 0.5 c.c. of sodium fluoride solution,

* With regard to the apparatus and graduated flasks required the original should be consulted.

and water to 5 c.c. is added; as much as will go on the point of a knife of sodium potassium tartrate is dissolved in the mixture, 4 c.c. of diluted liquor ferri dialysati are added and the mixture is centrifugalized for five to ten minutes. In the meantime the dilution of solution IV. is prepared by mixing 5 c.c. of the stock solution with sufficient distilled water to make 50 c.c. Further, 2 c.c. of solution I. and 2 c.c. of solution II. are introduced into a small Erlenmeyer flask. 5 c.c. of the liquid separated by centrifugalization, which must be quite clear and free from albumin, are added to the mixture of solutions I. and II., the contents of the flask are heated to boiling, on a piece of wire gauze, and allowed to boil for exactly three minutes. The flask is placed in cold water to cool, the precipitate of cuprous oxide is collected on a suitable filter (Allihn's filtering tube), washed with sufficient water, and then dissolved in 3 c.c. of solution III. The filter is washed with water which is allowed to run into the resulting solution so as to yield 10 to 12 c.c. of filtrate. It is now titrated with the solution of potassium permanganate until a faintly pink colour appears. From the amount of solution of potassium permanganate used the corresponding amount of copper is calculated, and by the aid of a table elaborated by the author the corresponding amount of sugar is ascertained. The method is said to yield sufficiently accurate results.

Sulphur Preparations (Colloidal Sulphur, Sulfidal, Sulfoform).

As a result of his investigations K. Hedén reports that colloidal sulphur is a gonococcide; however, its therapeutic value is inferior to that of the silver-albumin preparations and it is therefore not of practical use. Nevertheless, the results of his investigations are of theoretical interest inasmuch as they show that sulphur, which has so far been used as an antiparasitic only in dermatological practice, also acts as an antigonorrhœic. In anterior urethritis a 1·5 to 4 p.c. solution was used for injections, and a 0·5 to 1 p.c. solution for Janet's irrigations in anterior and posterior urethritis without complications; and a 1 to 2 p.c. solution for irrigations in gonorrhœa in women.

Sabbatani reports that on intravenous injection colloidal sulphur displays a toxic action, which he ascribes to the conversion of sulphur into sulphhydrate within the body.

Sulfidal, according to H. Winkler, is colloidal sulphur with a content of 25 p.c. of albuminous substances, and on account of its chemical characteristics is free from the drawbacks attending the use of sulphur. He used it in the form of an ointment prepared with glycerin for the treatment of scabies. It was applied in a thin layer which soon dried on the skin. The itching was relieved after the first or second application, and even severe suppurating secondary eczemas with pustules healed under this protective coating. The author directs that the ointment be applied once daily on three to five consecutive days, and on the fifth day it is removed by means of salicylic-vaseline. In mild cases of scabies and eczema healing is effected by this treatment in from eight to ten days.

M. Joseph advocates a more extensive use of colloidal sulphur in dermatology. In mild cases of seborrhœa of the face he used a 2 to 5 p.c. aqueous solution for washing the face, and gradually increased the strength to 10 p.c. For the treatment of acne indurata faciei he recommends a mixture of 10 grammes ($\frac{1}{3}$ oz) and 90 grammes (3 oz) of Lassar's salicylic paste, and should dermatitis supervene it may be replaced by a mixture of 10 grammes ($\frac{1}{3}$ oz) of sulfidal, 2 grammes (30 grains) of salicylic acid and 100 grammes ($3\frac{1}{2}$ oz) of white American vaseline. As a substitute for Vlemingkx's solution in the treatment of acne dorsi a solution of 50 grammes ($1\frac{3}{4}$ oz) of colloidal sulphur, 150 grammes ($5\frac{1}{4}$ oz) of soft soap in 350 grammes ($12\frac{1}{4}$ oz) of water can be used. This solution can likewise be employed in alopecia seborrhoica pityrodes, in addition to a 10 p.c. solution of sulfidal perfumed with oil of rose. In pityriasis rosea and eczema squamosum he prescribes a mixture of 10 grammes ($\frac{1}{3}$ oz) of sulfidal, 20 grammes ($\frac{2}{3}$ oz) of zinc oxide, 20 grammes ($\frac{2}{3}$ oz) of starch, 30 grammes (1 oz) of glycerin and 100 grammes ($3\frac{1}{2}$ oz) of water. Stronger ointments (20 to 50 p.c.) are required in the treatment of scabies and prurigo.

Sabbatani, Presse médicale 1913, No. 20, p. 191.

Winkler, Dermatologische Wochenschrift 1913, No. 12, p. 333.

Joseph, Dermatologisches Zentralblatt 1913, No. 12.

The therapeutic value of sulfoform* in the treatment of alopecia seborrhoica is discussed by M. Joseph, A. Sternthal and H. Merz. When using this preparation in an oily or alcoholic solution Sternthal at first observed a good action, but on stopping the treatment the disease continued its course. In sycosis non parasitaria the author employed the tannin zinc sulphide paste (5:10:100) proposed by P. Rosenthal, and a mixture containing sulfoform in the place of sulphur. Comparative tests showed that the mixture containing sulfoform was superior to that containing sulphur. Sulfoform also proved effective in scabies, in which the author made use of the following prescription: Rp. Sulfoform 25 grammes, pot. carb. 12.5 grammes, Vaseline 150 grammes; or, Rp. β -naphthol 15 grammes, sulfoform 10 grammes, cretae precip. 10 grammes, sap. moll. 50 grammes, vaseline 100 grammes.

In parasitic eczema the application of a 10 p.c. sulfoform-zinc paste containing 5 p.c. of pittylen always displayed a surprisingly rapid curative effect. On the other hand, in sycosis trichophytina and in acute weeping eczema sulfoform did not prove superior to other remedies. It proved especially effective in the non-callous form of chronic dry eczema, in which the author prescribed the following paste: Rp. Acid. salicyl. 2 grammes, tumenol ammon. 4 grammes, sulfoform 4 grammes, past. œsyp. ad 100 grammes. In combination with other appropriate drugs sulfoform yields good results in acne, pityriasis rosea and in impetigo.

Joseph considers sulfoform to be the best preparation of sulphur at present known for the treatment of alopecia seborrhoica, and he ascribes the incomplete results obtained by Sternthal to insufficiently prolonged treatment and to the small number of cases treated. Merz likewise comes to the same conclusion regarding the efficacy of sulfoform. He employed the preparation in the form of ointments, oily solutions, and in a fatty suspension.

Sulphuric Acid.

John Reynolds and Russell J. Reynolds state that they have used dilute sulphuric acid B. P. with uniform success

* Compare Merck's Reports 1910—1912.

Joseph, Dermatologische Wochenschrift 1913, No. 9, p. 255.

Sternthal, ibidem 1913, No. 6, p. 162.

Merz, Dermatologisches Zentralblatt 1913, No. 1.

Reynolds, Lancet, March 15, 1913, p. 749.

in the treatment of pyogenic infections, so that their method deserves further trial in the treatment of carbuncles, furuncles, staphylococcic and streptococcic infections, and also in bronchiectasis and pulmonary tuberculosis where there is a staphylococcic infection. The authors used the dilute sulphuric acid of the British Pharmacopœia, which has a specific gravity of 1.094 and a content of 13.65 p.c. of H_2SO_4 . They administered internally dilute sulphuric acid B. P. in doses of 20 to 30 minims, each dose diluted with 60 c.c. (2 oz) of water, every four hours. Externally carbolised vaseline (1 in 20) was applied.

In carbuncles treated by this method the following changes were observed. Within 24 hours the infiltrated area of tissue becomes strictly circumscribed; then the slough is observed to soften; during the next few days pus is freely discharged, and the whole affected area shrinks and healthy granulation tissue forms, filling up the cavity until the part is healed. The authors state that cicatrisation takes place in a comparatively short time.

In infected wounds, such as those resulting from abrasions, punctures, or inoculation by decomposing animal matter, treatment by dilute sulphuric acid also yields good results. The early symptoms of septicæmia rapidly disappear, the high temperature is quickly reduced and the pains and swelling gradually subside.

Recurrent crops of boils and severe cases of acne likewise yielded readily to treatment by dilute sulphuric acid; milder cases, e. g., blind boils, were aborted. The authors state that in tuberculous cases the fluctuations of temperature are influenced and the amount of sputum is diminished.

Tannalbin.

For the purpose of facilitating the administration of tannalbin* to children Sittler recommends the following mixture, which is readily taken on account of its chocolate-like taste:

* Compare Merck's Report 1908, p. 332.

Sittler, Schlesische Ärzte-Korrespondenz 1913, p. 210.

Rp. Tannalbin. 50 grammes
Cacao exoleat. pulv. 47 „
Pulv. aromat. 2 „
Saccharin. 1 „
Vanillin. 0.1 „

M. Ft. pulv. Sig.: To be taken as directed.

O. Hesse has undertaken an experimental study of the influence of tannalbin on the digestive movements in artificially produced diarrhoea in cats. He found that in animals not suffering from diarrhoea tannalbin exerts no marked influence, and only slightly delays the emptying of the stomach. In diarrhoea due to milk tannalbin has no effect on the consistency of the motions, which are not delayed. The motions in diarrhoea caused by castor oil likewise show no alteration, or only very rarely. In diarrhoea produced by colocynth tannalbin causes a slight alteration in the consistency of the fæces, but only in the minority of cases evacuation is delayed. On the other hand, the stools after the diarrhoea has passed off are usually constipated. In this case the point of attack of the action of tannalbin and of colocynth lies in the large intestine. Tannalbin does not prevent the display of the action of senna; on the other hand, diarrhoea produced by feeding with bread and organs of horses (spleen or liver) is influenced inasmuch as the fæces become firmer. X ray examinations showed that a surprisingly slight change in the duration of the digestive movements occurred during the display of the constipating effect of tannalbin on diarrhoea produced by colocynth or by bread and organs of horses. He therefore ascribes the mechanism of the action of tannalbin to its astringent action on the mucous membrane.

Tannismut.

Th. Petrina holds that tannismut* (bismuth bitannate) is a good intestinal astringent, the action of which extends to the whole length of the intestinal tract, without producing any undesirable secondary effects. He used it in acute, subacute and chronic catarrhs of the small and large intestine, and obtained uniformly gratifying results. In acute manifestations

Hesse, Archiv der gesamten Physiologie 1913, Vol. 151, p. 363.

Petrina, Therapie der Gegenwart 1913, No. 7.

* Compare Merck's Report 1912, p. 438.

the drug promptly displays an astringent effect after a few doses, the watery stools cease and soon assume a firm consistency. In subacute and chronic forms an improvement soon manifested itself after several days' administration of the preparation, and if given for a sufficiently prolonged period a cure was obtained. The use of tannismut has the advantage that a relapse need not be feared if it is administered for a prolonged period and an appropriate diet is given. The author gave 0.5 gramme ($7\frac{1}{2}$ grains) three to five times daily. M. Allina obtained equally good results.

Tannismut appears to have proved extremely useful in children's practice, judging from the communications by V. Pexa, R. Monti, H. Schmidt and H. Hummel. For children of eight months to ten years of age Pexa prescribed 0.5 gramme ($7\frac{1}{2}$ grains) of tannismut two to four times daily, according to the child's age, and obtained very good results in acute intestinal catarrhs. He first administered a laxative, gave instructions for the diet, and reduced the dose as soon as the action set in, with a view to preventing constipation. Schmidt and Hummel tried daily doses of 0.5 gramme ($7\frac{1}{2}$ grains) of tannismut in infants with gratifying results.

A. Tobeitz states that tannismut yielded good results in mild cases of dysentery, but failed in severe cases, as did also uzara, suppositories of omnopon and enteroclysms.

Tartaric Acid.

In addition to other reagents, a solution of tartaric acid is also used for the detection of potassium salts. However, apart from the fact that this reagent is not very sensitive it has the drawback that the potassium bitartrate which is formed, and which dissolves with difficulty, is liable to form a super-saturated solution, thereby impairing the course of the reaction. To obviate this drawback L. W. Winkler recommends the use of powdered tartaric acid in the place of a solution

Allina, *Die Heilkunde* 1913, No. 20.

Pexa, *Casopis lekaruv ceskych* 1913, No. 30.

Monti, *Wiener medizinische Wochenschrift* 1913, No. 37.

Schmidt, *Klinisch-therapeutische Wochenschrift* 1913, No. 44.

Hummel, *Allgemeine medizinische Zentral-Zeitung* 1913, No. 50.

Tobeitz, *Deutsche medizinische Wochenschrift* 1913, No. 48.

Winkler, *Zeitschrift für angewandte Chemie* 1913, No. 29, p. 208.

of tartaric acid, as the small crystals of tartaric acid prevent the formation of a super-saturated solution. The author gives the following directions for carrying out the test:

About 0.5 gramme of crystalline sodium acetate is dissolved in 10 c.c. of the neutral liquid to be tested, or in a 5 p.c. solution of the salt to be analyzed, about 0.5 gramme of powdered tartaric acid is added to the mixture and the whole is well shaken. In the absence of potassium (ammonium, rubidium and cæsium) salts the resulting solution remains quite clear, as the powdered tartaric acid quickly dissolves. On the other hand, the presence of 0.2 p.c. of potassium ion causes the well-known precipitate of crystalline potassium bitartrate; with 0.1 p.c. of potassium ion it occurs after a delay of one to two minutes. As a precaution a blank test may be applied with solution of sodium chloride or water.

According to H. Reckleben Winkler's test contains a possible source of fallacy in that the potassium bitartrate may remain in solution if the prescribed concentrations are not strictly adhered to, or potassium bitartrate which has not gone into solution may erroneously be assumed to indicate the presence of potassium. The test is rendered more reliable by the use of a fairly concentrated solution of sodium bitartrate.

Tests for Blood.

The benzidine test still occupies a leading position among the clinical methods for the detection of blood. A new modification has been suggested by W. A. Groat who uses barium peroxide in the place of solution of hydrogen peroxide. His procedure is as follows: 5 c.c. of pure glacial acetic acid are placed in each of two very clean test-tubes and as much as will go on the point of a knife of benzidine (for the detection of blood) and an equal amount of barium peroxide are added. Slight liberation of gas (oxygen) takes place and the solution assumes a brownish-yellow to greenish-yellow colour. If a green colour develops this is a sign that the acetic acid employed is not sufficiently pure (con-

taminated with iron), or that the test-tubes were not properly cleaned, and the solutions must be freshly prepared with the greatest cleanliness, and using the purest acetic acid. Into one of the test-tubes 1 c.c. is added of the extract or decoction of the solid material to be tested. In the presence of blood a deep blue or green colour develops within a few seconds. The second test-tube serves as a control test, and its contents should show no change of colour. The author states that this test is extremely delicate since a greater amount of hydrogen peroxide is liberated and enters into reaction on dissolving barium peroxide in acetic acid than is the case on adding ordinary 3 p.c. solution of hydrogen peroxide. Moreover, there is no risk of the solution of hydrogen peroxide having lost its activity on account of long storage.

The use of perhydrit offers the same advantage. The test* is carried out as follows: 1 gramme of benzidine (for the detection of blood) is dissolved in 10 c.c. of concentrated acetic acid (sp. gr. 1.064) and 0.3 to 0.4 gramme of perhydrit is added to 1 c.c. of this solution. If a solution containing blood is added to this solution a blue colour is immediately seen. If small amounts of perhydrit are used, about 0.05 gramme, the change of colour from blue to violet takes place much more slowly than is the case when using a 3 p.c. solution of hydrogen peroxide, but it is more permanent and this may under circumstances be an advantage in comparative tests.

The guaiacum resin test is discussed by J. Boas, B. Bardach, L. de Jager and E. Schaer. Boas modified his test by using a more suitable preparation for extracting faeces containing blood, and which consists of a mixture of 25 parts of glacial acetic acid and 75 parts of absolute alcohol. A specimen about the size of a bean of the faeces to be

* Compare Merck's *Prüfungsbuch der chemischen Reagenzien* 1912, p. 97.

Boas, *Berliner klinische Wochenschrift* 1913, No. 4, p. 154.

Bardach, *Chemiker-Zeitung* 1913, No. 118, p. 1190.

de Jager, *Nederlandsch Tijdschrift voor Geneeskunde* 1912, II, p. 237.

Schaer, *Schweizer Wochenschrift für Chemie und Pharmazie* 1913, p. 431.

tested is rubbed down in a porcelain capsule with "acetic alcohol" (i. e., the above mixture) and filtered through a small filter. If the filtrate has a dark brown colour 2 or 3 c. c. of alcohol are added. Finely powdered guaiacum resin is dissolved in alcohol to form a solution with a faintly yellow colour, 10 to 15 drops of which are added, without shaking, to the alcoholic extract of fæces, whereupon 20 drops of 3 p. c. solution of hydrogen peroxide are added. A positive reaction is apparent by the occurrence of a blue to violet coloration. The test can also be carried out with the dried filter, indeed here it is often even more distinct.

Bardach proposes the following modification of the guaiacum test. 3 drops of acetic acid (30 p. c.) are added to about 5 c. c. of urine and the mixture is allowed to stand for about two minutes. By this means the sensitiveness of the reaction is materially increased. 2 drops of a saturated alcoholic solution of guaiacum resin are now added, the mixture is shaken and about 1 c. c. (0.5 gramme) of powdered sodium perborate is added. In rapid succession 3 c. c. of concentrated acetic acid (80 p. c.) are added, the whole is shaken, 2 to 3 c. c. of alcohol are carefully "layered" on, and 1 or 2 drops of pyridine are added. With a positive reaction a blue coloration develops in the layered portion, at first in the vicinity of the pyridine. According to the amount of blood present this coloration either assumes the form of small blue spots or of a broad ring, and appears either immediately or in two to three minutes. The colour disappears after some time. The above coloration differs in many points from a similar reaction produced by nitrites. The blood test is characterised by the gradual development of the blue colour, which remains for some time, at the junction of the liquids, or in the alcoholic layer. The lower layer is coloured only when a large amount of blood is present. The nitrite reaction shows a different behaviour. The blue coloration invariably develops in the lower layer, it appears immediately and disappears with equal rapidity, and only in the presence of large amounts a blue ring is formed which also quickly disappears.

De Jager uses a mixture of 5 drops of solution of sodium hydroxide and 5 c. c. of ether for the guaiacum test, for the purpose of neutralising the too acid reaction of the acetic

acid extract* and thereby facilitating the appearance of the blue colour.

Schaer undertook experiments with several samples of guaiacum resin prepared by different methods, and he found that a natural resin of good composition is superior to resin purified by alcohol, or extracted by means of alcohol from guaiacum wood. He states that the resin extracted by means of chloroform from the heart-wood of guaiacum yields the most delicate and stable tests, and therefore is to be preferred for analytical use.

R. F. Ruttan and R. H. M. Hardisty hold that orthotoluidine is the most suitable reagent for the detection of blood in faeces, urine, and stomach contents. For their tests they employed a 4 p.c. solution of o-toluidine in acetic acid. The test was carried out in the same manner as the benzdine test and is said to be ten times more sensitive than the latter.

E. Schlesinger and J. Jagielski have published a critical review of the value of blood tests, based on their experiences and investigations extending over several years. They state that all chemical tests for blood have a number of sources of fallacies with which the analyst must be thoroughly acquainted in order to guard against mistakes. In addition, for three or four days after the patient has been placed on a meat-free diet the disappearance or permanence of the blood reaction must be noted, and with contradictory results control tests should be undertaken. The authors hold that the guaiacum test is not delicate enough for the detection of minimal bleeding. The phenolphthalin test is considerably less sensitive than the benzdine test, and has the drawback that it presents more sources of errors than the other tests. The objection that the benzdine test is too delicate and too subtle was based on the use of methods of application which did not yield definite results. The benzdine test is by no means too delicate if applied according to the method** de-

* Compare Zentralblatt für innere Medizin 1912, Vol. 33, p. 621.

Ruttan-Hardisty, Biochemical Bulletin 1913, Vol. 2, p. 225. —

Canadian Medical Association Journal 1912, November.

Schlesinger-Jagielski, Medizinische Klinik 1913, No. 11, p. 415.

** Compare Merck's Reagenzien-Verzeichnis 1913, p. 2. — Deutsche medizinische Wochenschrift 1906, No. 36, p. 1444. In carrying out the test care must be taken to ensure the absolute clean-

scribed by Schlesinger and Holst; it possesses that degree of sensitiveness which has been found requisite in a clinical test for detecting minimal amounts of blood with the existing technique. In some cases the benzidine test yields a negative reaction already on the day after commencing the meat-free diet. In these cases there is reason for suspecting that the positive reaction is suppressed by processes at work in the intestinal tract. Schlesinger states that in cases of this kind the reaction may likewise prove negative in ulcerated scirrhus.

Tests, Clinical and Diagnostic.

H. Maruyama has published a preliminary communication on a reaction which may prove of use as a diagnostic test of paralysis. The test is based on an anaphylactic process and is performed as follows: 0.02 c. c. of human blood serum is injected subcutaneously into a guinea-pig and two or three weeks later the cerebrospinal fluid of the patient is injected, using 1.5 to 2 c. c. per 100 grammes weight of animal. With the cerebrospinal fluid of a paralytic the animal dies within a few minutes with spasms. In the case of other psychoses the injection of cerebrospinal fluid produces no reaction or only a very slight one, but never causes the death of the animal. On the basis of his experiments the author lays great weight upon the proper dosage of the cerebrospinal fluid, as the use of smaller doses than 1.5 to 2 c. c. does not give the reaction. So far the author has not established whether this reaction also occurs in tabes, cerebral syphilis, meningitis and generally in all cases in which there is an increased content of albumin in the cerebrospinal fluid.

A simple colorimetric method for the quantitative estimation of urobilinogen has been elaborated by Flatow and Brünell. 10 c. c. of urine, acidulated by adding a trace of tartaric acid, are twice shaken in a cylindrical separator with 50 c. c. of

liness of the test-tubes and the purity of the reagents. A blank test should always be made as a precautionary measure, which should yield no positive reaction during the time of carrying out the test, or the reagents should be mixed prior to adding the material containing blood. Compare Merck's Report 1906, p. 57.

Maruyama, Wiener klinische Wochenschrift 1913, No. 30, p. 1233.
Flatow-Brünell, Münchener medizinische Wochenschrift 1913, No. 5, p. 234.

ether. The ether is run into a glass-stoppered cylinder and 4 c.c. of a 1 p.c. ethereal solution of dimethylamidobenzaldehyde are added, and after shaking, 6 to 8 drops of absolute alcohol saturated with hydrochloric acid. The whole is well shaken for three minutes, whereupon a certain amount of water is added (3—10 c.c. for urine with a normal content of urobilinogen, and 20—100 c.c. for urine with an increased content). The water should remove all the drops of dye adhering to the walls of the container. The layer of water containing the dye, under the ether, is withdrawn by means of a pipette and a portion is placed in the tube of the colorimeter. The standard tint tube is filled with a solution of phenolphthalein 1:50 000 to which a trace of sodium carbonate has been added. The colour of the phenolphthalein solution is now compared with that of the dimethylamidobenzaldehyde-reaction fluid. For further details the original should be consulted.

Another method of detecting urobilin in urine is given by Th. Hausmann. It is based upon Bogomoloff's observation that urobilin yields a violet coloration, similar to that of the biuret reaction, with an alkaline solution of copper. Hausmann gives the following directions for carrying out the test: 40 drops of a 10 p.c. solution of copper sulphate are added to 20 c.c. of urine, whereby an alkaline urine becomes acid. At first the urine assumes a green colour, and usually a more or less abundant precipitate of a light brownish-green colour is formed. About 2 c.c. of chloroform are now added and the whole is carefully mixed without shaking. If the urine contains urobilin the chloroform is coloured pink, or orange or copper-red, if the urine is very acid a yellow colour appears. The greater the amount of colouring substance present the more pronounced will be the yellow coloration; in the presence of very small amounts a pink tint is seen. The chloroformic solution of the colouring substance shows a characteristic absorption band in the spectrum (urobilin band).

Grigaut describes a very simple test for detecting urobilin and bilirubin in fæces. The fæces to be tested is mixed

Hausmann, Zeitschrift für experimentelle Pathologie 1913, Vol. 13, p. 380.

Bogomoloff, compare Neubauer-Hupperts Analyse des Harns 1913, II., p. 1382.

Grigaut, Revue internationale de médecine et de chirurgie 1913, No. 8, p. 133.

with boiling water, hydrochloric acid and then very dilute solution of ferric chloride are added. In the presence of urobilin a red to reddish-brown colour appears, and a green colour if bilirubin is present. This test is said to be a useful aid to diagnosis.

C. Lange has elaborated a test for the diagnosis of syphilis and paralysis. It is based upon the fact that after diluting the cerebrospinal fluid with a 0.4 p.c. solution of sodium chloride the red coloration produced by the addition of gold sol (solution of colloidal gold) is not altered, whereas in pathological conditions in definite dilutions a flocculent precipitation of the gold sol takes place. For this purpose the cerebrospinal fluid is diluted in series commencing with 1:10 and ending with 1:20 000, or 1:100 000. The degree of dilution at which the maximum precipitation occurs is noted, as in different affections the maximum reaction occurs at different dilutions and thus makes it possible to distinguish between different affections. This method was tested by Jaeger who obtained very satisfactory results. He states that the strongest reaction is given by cases of cerebrospinal syphilis, paralysis and tabes. In tabes it is not constant; on the other hand, he also saw a marked precipitation in a case of cerebral abscess consequent on a bullet wound, and weaker reactions in multiple sclerosis and in functional neuroses. For differential diagnosis the author considers it of importance that in syphilis the strongest reaction occurs in the higher dilutions. As a positive reaction occurred in 100 p.c. of the cases of paralysis, he concludes that Lange's test is more reliable than the Wassermann reaction. This is questioned by Zabziecki, who has likewise studied this test. Since the reliability of Lange's test depends on the proper composition of the solution of gold, H. Eicke gives the following directions for its preparation: 1 litre of quite freshly distilled water, 10 c.c. of a 1 p.c. solution of gold chloride and 5 c.c. of a 5 p.c. solution of glucose are heated to boiling. Immediately the mixture begins to boil a 5 p.c. solution of po-

Lange, Berliner klinische Wochenschrift 1912, p. 897.

Jaeger, 18th Meeting of psychiatrists and neurologists of Central Germany, Halle, October, 1912. — Zentralblatt für die gesamte innere Medizin 1913, Vol. 5, p. 282.

Zabziecki, *ibidem*.

Eicke, Medizinische Klinik 1913, No. 49, p. 2713.

tassium carbonate is added drop by drop until the boiling liquid assumes a dark colour; as a rule about 3.6 to 4 c.c. are required. A correctly prepared solution of gold should appear as a clear fluid with a deep purple colour, and will keep for months. Freshly distilled water must be used for all the solutions required in its preparation. The author also gives exact directions for carrying out the test. Since the test is very delicate and specific he believes that it is destined to fill a gap in the methods of examination so far available.

Another test for syphilis, which is deserving of interest on account of its simplicity, is described by W. Landau. It probably depends on the property of syphilitic blood serum of binding more iodine than normal serum. In addition to the patient's blood serum two reagents are required — the so-called iodine-oil reagent and the solution of starch. To prepare the iodine-oil reagent commercial white paraffin oil is used (not the pure official liquid paraffin). It must always be freshly prepared by rubbing down in a glass capsule 0.025 gramme of iodine with 0.2 gramme of alcohol by the aid of a glass rod and mixing the solution with 50 c.c. of white paraffin oil; the resulting iodine oil has a reddish-violet colour. The solution of starch which is used as an indicator is prepared in the usual manner (iodometry). The test is carried out as follows: The test-tubes (10 cm. in length and 0.8 to 1 cm. wide) are provided with a mark showing 2.7 c.c. (corresponding to 0.2 c.c. of serum + 2.5 c.c. of reagent). 0.2 c.c. of the serum to be tested is placed in the test-tube, which is then filled up to the mark with the reagent. The iodine reagent should not be measured with a pipette as it adheres too strongly to the glass. The test-tube is well shaken, whereby the iodine oil is more or less decolorized; it is then closed with an indiarubber stopper and kept in a horizontal position in a dark place at ordinary temperature. According to the time required for the reaction to take place, which must be previously ascertained for each batch of oil, a few drops of solution of starch are added after two to four hours. Normal sera assume a deep bluish-black colour, while with syphilitic sera the mixture retains its light yellow colour unchanged. Faintly positive sera show traces of a bluish coloration. As a safeguard a control test can be carried out

at the same time with normal serum. The author states that the only variable component of the iodine-oil reagent is the paraffin oil, since the rate of the reaction depends in a certain measure upon its composition. With the amounts and specimens of paraffin oil used by the author the best results were obtained when two and a half hours were allowed to elapse before adding the solution of starch. The various paraffin oils tested by the author differed only in regard to the rate of reaction. With several samples of oil the reaction was completed only after four hours. Therefore it is advisable first to ascertain the time of reaction of the paraffin oil employed.

St. von Bogdándy gives a simple method for estimating the amount of halogen in blood. As with the Kjeldahl method, the blood to be examined is treated with fuming sulphuric acid and at the same time air is passed into the apparatus, which carries with it the halogen hydrides which are then absorbed by a solution of silver nitrate. The amount of halogen silver formed is determined by the gravimetric method.

A simple method for the determination of the phagocytic index is described by B. Stuber and F. Rütten. It is designed to afford valuable information regarding the resistance and capability of reaction of the organism during the course of infectious diseases. The reagent used consists of a specially prepared suspension of spores of *Oidium albicans* in artificial serum (= 7.5 grammes of sodium chloride, 6 grammes of sodium citrate and water to 1000 grammes) to which ovo-albumin is added. The test is performed as follows: 0.1 c. c. of artificial serum, 0.1 c. c. of ovo-albumin solution, 0.03 c. c. of suspension of *Oidium albicans* and 0.03 c. c. of patient's blood are placed in a small centrifuge tube and are well mixed by means of a platinum needle. The mixture is placed for 45 minutes in an incubator at 37° C. and then centrifugalized for about one minute (at 800 revolutions). Too violent and too prolonged centrifugalization should be avoided. The majority of the red blood corpuscles collect in the capillary end of the tube, over them the leucocytes and over the latter the serum. The serum is now withdrawn by means of a capillary pipette, the capillary end (about 0.5 cm.

in length) of the tube with the erythrocytes is broken off, the remainder of the leucocytes in the tube are blown on to a slide and stained with Leishman's stain.

To render the method more simple I now supply "Stuber's phagocytosis reagent" in a stable form in ampoules. Each ampoule contains the mixture required for applying the test; the contents of one ampoule suffice for three tests. All that is necessary is to place 0.23 c. c. of the contents of an ampoule, previously well shaken, into a centrifuge tube, add 0.03 gramme of blood and carry out the test as described above. In the stained preparation the spores of *Oidium albicans* are stained a deep blue and are clearly demarcated by a white ring from their surroundings, so that there is no difficulty in counting them beside the leucocytes. To determine the phagocytic index the index of the emulsion of spores of *Oidium albicans* is first exactly determined for healthy individuals. For this purpose the number of spores of *Oidium albicans* situated in 200 leucocytes is determined; if, for instance 200 spores are counted in 200 leucocytes the quotient would be:

$$\frac{\text{Number of leucocytes}}{\text{Number of spores of } Oidium\ albicans} = 1 = \text{normal index.}$$

Using the same standard solution the patient's index is determined in exactly the same manner, the quotient then reads

Patient's index

$$\frac{\text{Patient's index}}{\text{Index of healthy individual (normal index)}} = \text{phagocytic index.}$$

The original paper contains several references to the diagnostic use of this method.

To test the renal function intravenous injections of a solution of milk sugar have been used according to Ullmann and Nonnenbruch, whereby the elimination of sugar is determined by chemical or polarimetric means. However, the elevation of temperature which followed the injection proved a drawback. Schlayer states that this symptom is not due to the milk sugar but to the presence of mould fungi in the preparation used. Therefore, the milk sugar should be stored in such a way as to prevent mould fungi from having access, and the solution should be sterilized in a steam sterilizer at a temperature of 100° C. for one hour. The elimination of

Schlayer, *Deutsches Archiv für klinische Medizin* 1910, Vol. 101, p. 345 and *Münchener medizinische Wochenschrift* 1913, No. 15, p. 800.

sugar by the kidneys should not be determined quantitatively, but by the aid of the polarimeter. For details of the method and its value the original should be consulted.

For testing the efficiency of the pancreas Winternitz recommends the use of mono-iodobehenic acid ethyl ester, an oily liquid containing 25 p. c. of iodine, which is not split up in the digestive tract if given on an empty stomach, so that no iodine can be demonstrated in the urine after three to five hours. However, if the same amount (3—4 c. c.) is given with food, three to five hours later the urine gives the iodine reaction. This proves that the secretion required to hydrolyse mono-iodobehenic acid ethyl ester — Winternitz's diagnostic — is liberated only when the function of the pancreas is stimulated by the ingestion of food. This diagnostic was submitted to an exhaustive test by P. Syring, who came to the following conclusion. If the iodine reaction of the urine remains absent during the twenty-four hours following the simultaneous ingestion of 5 c. c. of the diagnostic and of food, this is a certain indication of pancreatic insufficiency. On the other hand, it is not yet proved that a positive reaction denotes a normal condition of the pancreas.

The value of the Winkler-Schultze oxydase* reaction for the diagnosis of acute leukæmia, in which dimethyl-p-phenylenediamine and α -naphthol are the reagents used, is discussed by Haticgan, Raubitschek, Dunn and Rabe. In a series of investigations of the cerebrospinal fluid St. Scécsi found that the following constants are observed in the appearance and disappearance of the reaction: The oxydase reaction is positive in all diseases in which microlymphoidocytes and microleucoblasts, i. e., histogenous inflammatory tissue lymphocytes, are found in the cerebrospinal fluid. This applies particularly to paralytic dementia and tabes dorsalis, in which a positive reaction always occurs. On the other hand, a negative

Winternitz-Syring, Dissertation Leipzig 1913.

Haticgan, Wiener klinische Wochenschrift 1913, No. 14, p. 537.

Raubitschek, Zeitschrift für experimentelle Pathologie 1913, Vol. 12, p. 572.

Dunn, Quarterly Journal of Medicine 1913, Vol. 6, p. 293.

Rabe, Zeitschrift für experimentelle Pathologie 1913, Vol. 13, p. 371.

* Merck's Wissenschaftliche Abhandlungen No. 12.

Szécsi, Deutsche medizinische Wochenschrift 1913, No. 52, p. 2558.

reaction is the rule in acute inflammatory meningitis, in cerebral syphilis, in latent syphilis, etc., i. e., in diseases in which polynucleosis or a purely hæmatic lymphocytosis is found in the cerebrospinal fluid. Szécsi states that the reaction is a very reliable means of deciding whether paralytic dementia or cerebral syphilis is present. It is easily carried out: The side of the slide with the still moist swab is held for five minutes over a bottle containing formaldehyde (40 p.c.). The air-dried swab is now treated according to Schultze's modification B, i. e., it is placed for three to five minutes in a mixture consisting of equal parts of a 2 p.c. aqueous solution of microcidin and of a 1 p.c. aqueous solution of dimethyl-para-phenylendiamine hydrochloride. The preparation assumes a deep blue colour, and is examined, under water, under the microscope. In the positive cells small and larger granules with a blue to bluish-green colour are seen.

Thigenol.

A. Hirschberg reports on the use of thigenol* in gynæcological practice. In all those cases in which it was desirable to allay subacute and chronic inflammation of the pelvic cellular tissue, of the appendages or of the pelvic peritoneum, tampons impregnated with 20 p.c. thigenol-glycerin were introduced at regular intervals. With this treatment the author aimed at influencing residues of inflammatory intra-peritoneal or extraperitoneal exudates and their secondary manifestations in the neighbouring organs. He attached less value to effecting a cure of recent inflammations, in which thigenol tampons per se usually proved ineffective. In subacute and chronic processes the tampons were applied every second day, and the patients were instructed to remove the tampon on the following day and then irrigate with a mixture of two tablespoonfuls of thigenol-glycerin and 1000 c.c. of warm water. With this treatment, assisted by appropriate dietary rules, the pains were quickly relieved and the manifestations subsided.

J. Garnmann states that thigenol is a useful remedy for itching, especially in urticaria. He painted the affected parts with a 5 p.c. aqueous solution of thigenol, with the

Hirschberg, Berliner klinische Wochenschrift 1913, No. 13, p. 597.

* Compare Merck's Reports 1902 and 1912.

Garnmann, Therapie der Gegenwart 1913, No. 4, p. 191.

result that the distressing itching disappeared in the course of five to ten minutes, and after fifteen minutes all the wheals likewise disappeared. A slight relapse which occurred on the following evening responded with the same success to this treatment. Thigenol also proved a good remedy in other forms of pruritus, inter alia in an old woman who had suffered for years from pruritus cruris associated with varicose eczema of the leg. The anti-urticarial effect of thigenol is explained by the fact that in inflammatory affections thigenol, thiol and ichthyol all display an absorbent, antiphlogistic, astringent action, in addition to producing bloodlessness of the part.

F. Kubaschewski used thigenol per se and in the form of a 10 p.c. ointment in veterinary practice. He states that it yielded good results in malanders and in injuries to the hoofs in horses.

Thiocol.

J. G. Rey places on record his experience of thiocol in the treatment of tuberculosis in children and in whooping cough. In surgical tuberculosis he prescribed large doses of thiocol and a special diet consisting mainly of milk puddings, but milk was never given without cereals. The author states that if this treatment is strictly carried out spina ventosa, tuberculous affections of the hands and tarsus, blue cold abscesses, tuberculosis of the peritoneum, old-standing costal pleurisy with callosities disappear in the course of a few months without any surgical interference, and without undergoing treatment in a sanatorium or at the seaside. Even in infants with acute tuberculosis this therapy is said to arrest the malady. The use of thiocol, the author says, promises a certain cure in incipient tuberculosis in childhood, if no open visible tuberculosis is apparent, but its presence can be diagnosed by the practitioner. The stimulating action of the preparation on metabolism leads to a decided improvement in the patient's general health in cases where the weight remains stationary on account of latent tuberculosis, and likewise in chronic states of intoxication, such as frequently remain after severe disease of the intestines, pneumonia,

Kubaschewski, Berliner tierärztliche Wochenschrift 1913, No. 46, p. 817.

Rey, Therapie der Gegenwart 1913, No. 9, p. 397.

measles, whooping cough, etc., and which hinder the child's bodily development. With an appropriate diet a gain in weight manifests itself after a fortnight, while the tissue tonicity shows a progressive improvement, and after six to eight weeks' treatment a general recovery and gain in strength are evident.

The observation that children treated by thiocol remained free from whooping cough in spite of exposure to infection induced the author to try it in the treatment of whooping cough, in which it yielded very good results. He states that the preparation exerts a marked influence not only on the symptoms but also on the duration of the malady, and acts as a prophylactic to the lighting up of tuberculous foci, and also prevents the development of miliary tuberculosis, peritonitis, meningitis, etc. Rey states that thiocol is harmless and is well borne by infants one month old even in daily doses of 2.5 grammes (38 grains). It should be given at least 15 minutes before meals, in water with a little raspberry syrup or sugar. When severe paroxysms of coughing and vomiting were already present, the author gave an appropriate dose of codeine or omnopon half an hour before meals, after an artificially induced attack of coughing had passed off, and then administered thiocol. An improvement does not set in at once, but after three or four days; in cases in the convulsive stage an aggravation of the condition may even occur at first. The duration of the malady varies, and is influenced by the time of year and whether recourse was had to the drug at the beginning or in the advanced stage of the malady.

Thiol.

O. Nordmann holds that thiol is a valuable remedy for the treatment of burns. In burns of the first degree it is superior to ointments and fats on account of its property of readily absorbing moisture. At first the surrounding skin should be carefully cleansed with a pledget of cotton wool impregnated with benzin, and then painted with 5 or 10 p.c. tincture of iodine; if deemed necessary hairy parts may first be shaved. To spare the patient pain care should be taken that no benzin or tincture of iodine comes in contact with the wound itself. Thiol is now applied to the entire surface

Nordmann, Medizinische Klinik 1913, No. 34, p. 1383.

of the burn by means of a spatula which has previously been boiled, and the whole is covered by a layer of sterile gauze and a cotton wool dressing. The same procedure is followed in burns of the second degree, after pricking the blisters at the base with a sterile needle. Blisters which have burst should be snipped and removed with pincers sterilized by boiling. In burns of the third degree recourse should be had to dressings with xeroform and noviform in powder; if the burns cover over one-third of the surface of the body treatment in an hospital by permanent water baths is indicated.

The thiol dressings described in the foregoing are changed as often as the dressing is found to be impregnated with secretion, whereby the lowest layer of gauze is always allowed to remain in position. Further, when the dressing of thiol or powder has become dry it should be removed by means of a warm bath, as otherwise the change of dressing causes considerable pain. If on removing the dressing it is found that a part of the burn is covered with skin, treatment by thiol is limited to the still discharging parts of the wound. For further hints regarding the treatment and after-treatment of burns the author's original paper should be consulted.

Thorium X.

Towards the end of the past year K. Herxheimer reported the cure of a case of sarcomatosis of the skin by means of injections of thorium X*. However, according to a recent communication by the author this success was only transitory, and after some time metastases again developed and the patient died. Experiments undertaken by H. Hirschfeld and S. Meidner on rat sarcoma showed that thorium X was ineffective, or failed to exhibit a constant action. In ten cases of human carcinoma the results were negative; a certain amount of improvement was seen in sarcoma.

In a case of lymphosarcoma P. Krause injected 210 electrostatic units during the first six days, and 390 electro-

Herxheimer, Münchener medizinische Wochenschrift 1912, No. 47, p. 2563 and 1913 No. 4, p. 185.

* Compare Merck's Report 1912, p. 287.

Hirschfeld-Meidner, Zeitschrift für klinische Medizin 1913, No. 5, p. 407.

Krause, Berliner klinische Wochenschrift 1913, No. 13, p. 596.

static units in all in the course of three weeks. With this treatment he was able to observe a slight transient effect only at the site of injection into the tumour, whereas the net result was nil in spite of the large doses employed.

Thorium X treatment seems more promising in various skin affections. Nägeli and Jessner found that the local application of solutions by dropping yielded good results in psoriatic plaques, but in cases of neurodermatitis and lupus erythematosus the results were doubtful. Ointments showed the same behaviour, these were prepared by the authors by mixing a solution of thorium X with anhydrous lanoline, or thorium X powder and vaseline. Already a single application of this ointment in psoriasis led to a marked improvement in the foci, and concentrated ointments appear to have a particularly good effect. According to F. Gudzent and Winkler thorium X has not proved the remedy of choice in psoriasis, still it deserves consideration when other methods of treatment have failed.

The nature of the active principle of the biological action of rays, particularly with regard to the action of thorium X in gout, is discussed by J. Plesch, G. Schwarz, W. Falta and L. Zehner. For particulars the originals should be consulted as they cannot well be briefly abstracted. With regard to the value of thorium X in gout Falta reports that he succeeded in successfully treating a severe case of gout. It was that of a man who had suffered for thirteen years from recurring attacks. He was given 3 electrostatic units of thorium X three times daily, whereupon the patient's condition showed a surprising improvement, and the swellings of the joints markedly subsided.

Thorium X appears to have awakened most interest in the treatment of diseases of the blood, and its use in this indication is reported on by A. Bickel, G. Klemperer

Nägeli-Jessner, *Therapeutische Monatshefte* 1913, No. 11, p. 770.
Gudzent-Winkler, *Deutsche medizinische Wochenschrift* 1913, No. 20, p. 925.

Plesch, *Berliner klinische Wochenschrift* 1913, No. 4, p. 165.

Schwarz, *Berliner klinische Wochenschrift* 1913, No. 9, p. 396.

Falta-Zehner, *Berliner klinische Wochenschrift* 1913, No. 9, p. 395.

Falta, *Medizinische Klinik* 1913, No. 9, p. 349.

Bickel, *Berliner klinische Wochenschrift* 1913, No. 8, p. 346.

Klemperer-Hirschfeld, *Therapie der Gegenwart* 1913, No. 2, p. 57.

and H. Hirschfeld, Arneth, M. Tschernorutzky, F. E. Park, de Nobele, G. Rosenow, J. von Benczur and O. Meseth. The conclusion to be drawn from these publications is that the internal, subcutaneous and intravenous administration of this preparation holds out a promise of success especially in anæmias, leukæmias and in pernicious anæmia, although too much must not be expected, particularly in leukæmias. The fact must be taken into account that intravenous injections of thorium may cause hæmorrhages of the large intestine, which are due to the local action of thorium X when eliminated by the intestinal walls*.

Thorium Chloride.

A. Caan has undertaken experiments with thorium chloride in mouse cancer and rat sarcoma the results of which show that this preparation is capable to a certain extent of beneficially influencing and hastening the healing process. So far the good results reported by the author are exclusively based upon animal experiments, and clinical trials must be undertaken to ascertain whether the same effects are produced in man. Nevertheless, the results recorded by Caan encourage its trial in man. However, attention must be drawn to the fact that for his experiments the author did not use commercial thorium tetrachloride, but a product obtained during the process of preparing mesothorium and which contained traces of mesothorium. The injections were made into the tumour and yielded noteworthy results. The author states that he intends making trials with intravenous injections.

Arneth, Deutsche medizinische Wochenschrift 1913, No. 16, p. 733 and No. 17, p. 787.

Tschernorutzky, Internationale Beiträge zur Pathologie und Therapie der Ernährungsstörungen 1913, Vol. 4, p. 291.

Park, Medical Record 1913, Vol. 83, p. 429.

Nobele, Archives d'électricité médicale, July 10, 1913. — Revue de thérapeutique 1913, No. 15, p. 533.

Rosenow, Münchener medizinische Wochenschrift 1913, No. 40, p. 2214.

Benczur, Therapie der Gegenwart 1913, No. 10, p. 443.

Meseth, Münchener medizinische Wochenschrift 1913, No. 38, p. 2105.

* Compare G. Mayebo, Deutsche Medizinal-Zeitung 1913, No. 49, p. 786.

Caan, Münchener medizinische Wochenschrift 1913, No. 20, p. 1078.

Should these prove capable of exerting a therapeutic influence on malignant tumours, reference will be made to the results in a subsequent volume of my Reports.

Thymol.

Among the various remedies employed to destroy tapeworms thymol deserves consideration, although its tæniifugal value has been questioned. On account of its slight toxicity it is preferable, under certain circumstances, to the use of extract of male fern or pelletierine. S. Artault has obtained better results with thymol than with melon pumpkin seeds, since in his experience the large doses of the latter required to expel the tapeworm may cause digestive disturbances. He prescribed thymol *inter alia* in a recurrence of tapeworm in a patient who had suffered from dyspepsia after the administration of melon pumpkin seeds, and obtained a complete success. He states that no preliminary treatment, except total abstinence from alcohol, is required. 0.25 gramme (4 grains) of thymol in a cachet is given in the morning on an empty stomach, and this treatment is continued until it may safely be assumed that the head of the tapeworm has been expelled, or until it has been found in the fæces. This usually occurs on the third or fourth day. If the head has not been found this treatment is continued for a period of at least eight days. With this treatment the author always succeeded in expelling the tapeworm, without inconvenience or risk to the patient. The striking feature of this treatment is the small dose of thymol prescribed by the author, in contradistinction to Gampi, whose treatment for worms consists in giving the patient castor oil at night, and in the morning 0.666 gramme (10 grains) of thymol every quarter of an hour until 8 grammes (120 grains) in all have been taken, when castor oil is again administered. During the treatment a little rum or brandy may be taken.

W. Allan also reports three cases in which the use of thymol yielded excellent results. These were cases of *Tænia*

Artault, *Bulletin général de thérapeutique* 1913, No. 7. — *Klinisch-therapeutische Wochenschrift* 1913, No. 33, p. 979.

Gampi, compare Liebreich-Langgaard, *Compendium der Arzneiverordnung* 1907, p. 716.

Allan, *Journal of the American Medical Association* 1912, Vol. 59, p. 197.

saginata, which was expelled in every instance, without any recurrence.

Guillon also speaks in favour of thymol, and even considers it the best tæniacuge at present known. He prescribes a milk diet on the evening before its administration. On the following morning the patient is given three doses of thymol, in cachets, at hourly intervals. Adult males are given 1 gramme (15 grains) of thymol for a dose, women 0.75 gramme (11 grains), and children smaller doses according to their age. Three quarters of an hour after giving the last dose a laxative is administered, 30 to 50 grammes (1— $\frac{1}{3}$ oz) of sodium sulphate, but no oily or alcoholic preparations, e. g., no castor oil or compound tincture of jalap, as these dissolve the thymol and consequently give rise to undesirable secondary effects.

Schüffner and Vervoort report that thymol is also effective in ankylostomiasis. The authors gave 1 gramme (15 grains) of thymol every two hours, five doses in all, and two hours after the last dose 20 grammes ($\frac{2}{3}$ oz) of castor oil; or 2 grammes (30 grains) were given and this dose repeated after two hours, followed three hours later by a dose of 17 grammes of castor oil and 3 grammes of chloroform.

For the disinfection of the field of operation H. Köhler states that an alcoholic solution of thymol presents several advantages over the now much used tincture of iodine, which makes it especially useful in military medicine. In the first place it is less irritating, even to the scrotum and perineum, does not lead to idiosyncrasy, and in operations for goitre and Graves's disease is not followed by absorption of iodine, and in inflammatory processes such as lupus, hæmatoma and nævi does not interfere with the clinical picture of the malady, does not damage the linen to the same extent, and keeps for an unlimited period.

A. Jolles employs thymol to detect the presence of indican in urine. 2 c.c. of a 20 p.c. solution of lead acetate are added to 10 c.c. of urine, the mixture is filtered and

Guillon, Presse médicale 1913, No. 63, p. 644.

Schüffner-Vervoort, Münchener medizinische Wochenschrift 1913, No. 3, p. 130.

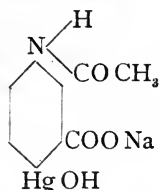
Köhler, Deutsche militärärztliche Zeitschrift 1913, No. 16.

Jolles, Zeitschrift für physiologische Chemie 1913, Vol. 87, p. 310.

0.5 c.c. of 10 p.c. alcoholic solution of thymol, 10 c.c. of hydrochloric acid containing ferric chloride (Obermayer's reagent) and 4 c.c. of chloroform are added to the filtrate. If indican is present the chloroformic layer assumes a violet colour on shaking. On shaking with water the colour changes to brownish-yellow or reddish-brown, and reappears on adding concentrated hydrochloric acid to the chloroformic layer.

Toxynon.

A new preparation of mercury, toxynon, is described by C. Gutmann. According to his report it is sodium acetamino-mercuribenzoate, with a content of 48 p.c. of mercury. It is with difficulty soluble in water, more soluble in solution of sodium chloride and in dilute solution of piperazin. Its chemical structure may be expressed:



Experiments undertaken by Blumenthal and Oppenheim show that the lethal dose of toxynon for a rabbit weighing 2.5 kilogrammes is about 0.15 gramme, hence it would be about half as poisonous as mercury salicylate.

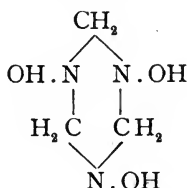
Toxynon is used in the form of intravenous injections in the treatment of syphilis. According to Gutmann's investigations preliminary treatment by toxynon, followed by the use of salvarsan, is especially advantageous. In a sterile isotonic solution it can be given daily or every second day in doses of 0.1 to 0.2 gramme. Apart from the action displayed by the preparation itself, the author lays stress upon the fact that after a course of toxynon treatment, usually lasting eight days, the injections of salvarsan are almost without exception well borne and do not give rise to any reaction. Fever, gastric and intestinal disturbances, headaches and other secondary effects referable to salvarsan treatment remained absent, although comparatively large initial doses of salvarsan were given.

Tributyrim.

Tributyrim is butyric acid glycerol ester, of the formula $C_3H_5(COO \cdot C_3H_7)_3$, a colourless oily liquid, which is not miscible with water. Exposed to damp air the preparation is partly hydrolysed with formation of glycerin and free butyric acid, whereby the rancid smell of the latter becomes apparent. Lipolytic ferments likewise cause the same decomposition, and H. Davidsohn's test to differentiate human milk from cow's milk is based upon this fact. If 1 or 2 drops of tributyrin are added to 5—10 c.c. of milk and the mixture is allowed to stand for a few minutes, shaking occasionally, in the case of human milk a penetrating odour of butyric acid becomes apparent, but this is not the case with cow's milk. However, if the ferment has been destroyed by boiling human milk no longer gives this reaction. Hence this test makes it possible to distinguish human milk from cow's milk, and also to distinguish unboiled from boiled human milk. The addition of a small amount of cow's milk to human milk cannot be detected by this test, but if the mixture consists principally of cow's milk, i. e., if the latter amounts to three-quarters of the whole, the reaction is negative. By the aid of the stalagmometer the author also came to the conclusion that human milk contains a very active lipase, traces of which only could be detected in cow's milk.

Trioximinomethylene.

Trioximinomethylene, or triformoxime, occurs as a white, amorphous powder, of the chemical formula $(CH_2:N_3 \cdot OH)_3$, or



It is insoluble in water and in the usual organic solvents, but is soluble in mineral acids and in solutions of caustic alkalis. It has no melting point, it volatilises slowly at $100^\circ C.$, more

quickly at 132° — 134° C., whereby it is converted into formoxime, $(\text{CH}_2:\text{N}\cdot\text{OH})^*$.

L. Lewin states that this preparation may be used as a test for albuminous substances. If albumin is shaken with a solution of 0.1—0.15 gramme of triformoxime in 100 grammes of crude sulphuric acid the mixture assumes a distinct violet colour within a short time. This reaction is produced by egg albumin, serum albumin, casein, peptone, papain, nucleoproteids, etc., but not by glue. This test is extremely delicate, and the reaction occurs on adding the reagent to 1—2 c.c. of a 0.05 p.c. solution of egg albumin. The limit of sensitiveness of the test is reached with a concentration of 0.02 p.c. of albumin. If the violet solution is sufficiently concentrated an absorption-band is seen at $\gamma = 536 \mu\mu$. The colour disappears on the addition of nitric acid or of hydroquinone. It may be mentioned that pure sulphuric acid should not be used for preparing the reagent, as the reaction depends upon the presence of a body contained in crude sulphuric acid, probably selenious acid or arsenious acid.

Para-formaldehyde (or trioxymethylene) may be used in the place of triformoxime; however, the colour produced is not so pure, nor so stable and delicate as with triformoxime. On the other hand, tyrosin reacts only to a mixture of para-formaldehyde and sulphuric acid, with a green colour, but not to a mixture of triformoxime and sulphuric acid.

Trivalin.

Overlach states that trivalin is the name applied to a combination of the valerianates of morphine, caffeine and cocaine, which is issued ready for use in ampoules of 1 c.c. (or 1.2 c.c.). Each ampoule contains 0.01935 gramme of morphine valerianate, 0.0037 gramme of caffeine valerianate, and 0.00506 gramme of cocaine valerianate. The author states that this combination has the advantage over morphine of not causing vomiting or nausea, further, it does not give rise to symptoms of cardiac paralysis or to any symptoms referable to the

* Compare R. Scholl, *Berichte der deutschen chemischen Gesellschaft Berlin* 1891, Vol. 24, p. 575.

Lewin, *ibidem* 1913, Vol. 46, p. 1796.

Overlach, *Zentralblatt für innere Medizin* 1912, No. 18, p. 422.

respiratory centre*. In addition, the action of morphine is displayed by trivalin in an intensified degree, so that trivalin should prove useful for combating all forms of pain, in painful procedures and in affections of old age, in which the use of morphine is contra-indicated on account of the possible occurrence of acute weakness. In this combination the action of iso-valerianic acid on conditions of nervous excitement is also intensified. Overlach's statements were on the whole confirmed by the results of the clinical investigation of trivalin undertaken by Mehliß. He has found the preparation a useful substitute for morphine in allaying pain, for instance, in effecting a change of dressings, before minor operations, and as a preliminary to cystoscopy. However, in a few cases it gave rise to gastric disturbances. As a rule Mehliß injected 0.5 to 1 c.c., and his patients stated that the pains were relieved or passed off after ten to fifteen minutes. In two patients who suffered great pain due to diabetic gangrene 1 c.c. of trivalin proved effective, whereas 0.01 gramme of morphine or 0.02 gramme of omnopon had failed to relieve the pain. O. Berneker and A. van Tienhoven also express a very favourable opinion of the analgesic action and ready tolerance of trivalin.

"Trivalin locale" is a modification of trivalin which was used by A. Glück as a local anæsthetic in minor operations.

* Overlach believes that vomiting, apart from idiosyncrasy, is caused by the formation of apomorphine and other poisonous derivatives of morphine on heating morphine in the presence of hydrochloric acid. However, he overlooks the fact that during sterilization of a solution of morphine hydrochloride the possibility of apomorphine being formed is excluded. H. Stenzl. (Zentralblatt für innere Medizin 1913, No. 3, p. 67) rightly draws attention to this fact. It has already been definitely established for some time that neither apomorphine nor chloromorphide are formed on heating solutions of morphine such as are used for subcutaneous injections. Nor can this take place when a solution of morphine is allowed to stand for a long time, and this fact has long been borne out by practical experience in the manufacture of morphine. Therefore it is time these entirely erroneous statements regarding the decomposition of solutions of morphine were omitted from the literature.

Mehliß, Deutsche medizinische Wochenschrift 1913, No. 14.

Berneker, Dermatologische Wochenschrift 1912, No. 45.

Tienhoven, Nederlandsch Tijdschrift voor Geneeskunde 1913, Vol. 57, I, p. 97.

Glück, Medizinische Klinik 1913, No. 39, p. 1597.

It contains in 1 c.c. 0.0048375 gramme of morphine valerianate, 0.0074 gramme of caffeine valerianate and 0.01012 gramme of cocaine valerianate, in addition to a little suprarenin. In minor operations a subcutaneous or intracutaneous injection of 1 to 2 c.c. usually produces after three or four minutes complete anæsthesia of sufficient duration. For more extensive procedures 2 to 3 c.c. are required, and these doses are well borne also by children. The author has used as much as 5 c.c. in adults without ever observing any disturbance of the general condition. Occasionally the strong odour of valerianic acid of the preparation was objected to.

Tropacocaine.

Further reports on the value of tropacocaine* in spinal analgesia have been published by A. P. Marjantschik, A. Hoffmann, H. Helm, R. Dax, P. Gorse, J. T. J. Morrison, K. Vogel, A. Kraemer, L. Zorn, Boncaglia and J. J. Ulrich Cuny.

Hoffmann gives valuable hints regarding the technique of spinal analgesia. He reminds the operator who wishes to induce spinal analgesia that in adults the spinal cord extends to the upper end of the second lumbar vertebra, in children a little lower, but never above the lowest border of the third lumbar vertebra. A syringe with a capacity of 10 c.c. is required, with a hollow needle 8 to 10 cm. in length and with a diameter of 0.8 to 1 mm., fitted with a stylet. The needle must be boiled in a solution of soda and then carefully cleansed with physiological salt solution to remove the soda. The patient should be in the sitting posture, if possible, and

* Compare Merck's Reports 1892—1912.

Marjantschik, *Annalen der Universität Kiew* 1913, Vol. 53, p. 139.
Hoffmann, *Medizinische Klinik* 1913, No. 49, p. 2013.

Helm, *Beiträge zur klinischen Chirurgie* Vol. 81. — *Zentralblatt für Gynäkologie* 1913, No. 26, p. 981.

Dax, *Beiträge zur klinischen Chirurgie* 1913, Vol. 83, No. 3.

Gorse, *Gazette des hôpitaux* 1913, No. 31, p. 488.

Morrison, *British Medical Journal* 1913, I, p. 1305.

Vogel-Kraemer, *Medizinische Klinik* 1913, No. 10, p. 369.

Zorn, *Zeitschrift für experimentelle Pathologie und Therapie* 1913, Vol. 12, p. 529.

Boncaglia, *Monatsschrift für Geburtshilfe und Gynäkologie* 1913, No. 2.

Cuny, *Dissertation Würzburg* 1913.

the needle with the stylet is inserted in the middle line between two spinous processes, between the fourth and fifth spinous processes, or third and fourth lumbar vertebræ. After passing through the interarticular cartilage the stylet is withdrawn and the needle is slowly pushed forward until drops of clear cerebrospinal fluid issue in rapid succession. If this is not the case the needle must be withdrawn and introduced in another direction, or its introduction must be repeated in another part, and if it is not possible to obtain the proper flow of cerebrospinal fluid in drops it is better to abandon the injection of the anæsthetic, since it is not likely to lead to a certain success. If it is not possible to make the injection into the median line, it is then made to the right or left of this line. If the cerebrospinal fluid is clear about 8 c. c. are aspirated into the syringe, into which 0.05 gramme of tropacocaine has been placed, whereupon the contents of the syringe are injected very slowly. The needle is then withdrawn and the puncture covered with sterile gauze. The patient is then placed in the Trendelenburg position, not too inclined, and after anæsthesia has set in he is transferred to the horizontal position, unless another position is required for the operation. In the author's experience it is possible to obtain by this method anæsthesia reaching to the level of the umbilicus, or closely below it. With proper technique Hoffmann never saw any unwelcome sequelæ and only in a very few cases headache occurred. As a rule, the anæsthesia or analgesia was excellent.

Helm also gives a very satisfactory account of his experience. Among 1419 cases the failures amounted to only 7.4 p. c., and he never saw any severe disturbances. In the opinion of many authors tropacocaine is not responsible for the unwelcome sequelæ which have been reported, but these must be ascribed to the spinal application. Vogel and Kraemer on the whole share this view. In a man, aged 75, after an uncomplicated operation for hernia under spinal analgesia they observed transient manifestations of disturbance of the vagus and bradycardia. If there exists a causal connexion between these disturbances and the lumbar injection then, in the authors' opinion, not only should caution be exercised in resorting to spinal analgesia — possibly limited to the use of tropacocaine — but the still obscure question of heart-block should be cleared up. Dax, who considers spinal analgesia a valuable

addition to operative technique, states that there is no justification for deprecating its use, but he is in favour of definitely establishing its indications. He advocates the use of spinal analgesia in aged persons, in the presence of cardiac defects, in diseases of the lungs (especially tuberculosis), in renal diseases and in diabetes, but deprecates its use in diseases of the central nervous system, in hysterical and neurasthenic subjects, and in all septic and suppurative processes. In agreement with most authors Dax prefers the use of tropacocaine for spinal analgesia, although it is not quite harmless. As a rule he employed a dose of 0.06 gramme (1 grain) of tropacocaine in 5 p.c. solution. He states that he obtained very good results. Morrison came to the same conclusion, whereas Marjantschik, who does not consider spinal analgesia per se to be quite harmless, advises its use only in cases where this method is definitely indicated.

In operations on the vagina and in laparotomies Boncaglia made use of a combination of tropacocaine and strychnine for lumbar anæsthesia. He injected 0.05 gramme ($\frac{3}{4}$ grain) of tropacocaine and 0.001 gramme ($\frac{1}{64}$ grain) of strychnine, and never saw pyrexia which might he attributed to this method of inducing anæsthesia. Headache was an infrequent sequela. The author recommends his method for all gynecological operations.

An explanation for the favoured position occupied by tropacocaine is afforded by Zorn's table according to which cocaine is the most powerful local anæsthetic, followed in turn by tropacocaine, novocaine, stovaine, alypin, and eucaine. M. Kochmann uses 2 to 3 p.c. solutions of tropacocaine for instillations into the eye, and solutions containing 0.1 to 0.2 p.c. in a 0.9 p.c. solution of sodium chloride for Schleich's infiltration anæsthesia, and for spinal analgesia about 0.05 gramme ($\frac{3}{4}$ grain) in 0.5 p.c. solution. The author draws attention to the use of tropacocaine in tabetic crises, by means of which the pains are abolished for twenty-four hours or longer.

Ulrich Cuny, who has used spinal analgesia in fifty cases in gynecological practice, expresses himself as follows with regard to spinal analgesia in general and the use of tropacocaine in particular: Spinal analgesia is an extremely

valuable addition to existing methods of inducing anæsthesia. In operations on the lower half of the body perfect anæsthesia lasting about one hour can be induced in suitable cases, whereby the patient's age must be taken into account. However, the greatest care must be observed in the technique and tropacocaine should be used, which may be considered the least harmful of all preparations used for this purpose, in combination with a mild scopolamine-morphine dawning sleep. Failures are due in almost every instance to a mistake in making the puncture. Alarming symptoms, especially those referable to respiration, can be prevented by slowly aspirating and injecting, and also by allowing at least fifteen minutes to elapse between the injection and placing the patient in the Trendelenburg position. In the author's opinion this method has the further advantage that the operator can, if necessary, obtain the patient's consent to carry out a more extensive operation than originally contemplated, should the necessity for such a step become apparent during the performance of the operation. In addition, it must be taken into account that the patient's condition after the operation is on the whole better than following the use of general anæsthesia. Vomiting and headache are rare sequelæ, and when present occur in a mild form; and no deleterious effect on the lungs and heart, as is the case after the use of chloroform-ether, or on the kidneys and emptying of the bladder, was seen. The pyrexia which occurs during the first few days after the operation is, in the author's opinion, more likely due to absorption fever than to the method, and it never proved harmful to the patients. Ulrich Cuny lays stress upon the fact that not a single death occurred which could be attributed to the use of spinal analgesia. Hence he regards it as an invaluable gain to gynæcology with its limited field of operation.

Tryen (Yatren or Xantropin).

O. Anselmino undertook a study of the constitution of tryen, or yatren, as it has recently been called. According to the statements in the literature this preparation is said to be p-iodo-o-sulpho-oxycyclohexatrien pyridine*. Anselmino holds that the designation cyclohexatrien pyridine is an inaccurately

Anselmino, Apotheker-Zeitung 1914, No. 1, p. 10.

* Compare Merck's Report 1912, p. 455.

formed designation for chinoline, and its use in the above mentioned description for this iodine substitution product tends to obscure its actual constitution. According to this author's investigation yatren consists solely of a mixture of 8-oxy-7-iodo-chinoline-5-sulphonic acid with 20 p. c. of sodium bicarbonate, therefore Anselmino is of opinion that this preparation is identical with new griserin*, which in turn is probably isomeric or identical with loretin**. Since an oxy-iodo-chinoline sulphonic acid is again being introduced into materia medica, and, as was the case at the time with griserin and loretin, will be prescribed by practitioners, Anselmino thinks that the time has come to investigate the isomeric oxy-chinoline sulphonic acids, in view of the fact that reliable data regarding these products cannot be found in the literature. As is apparent from the communications by the authors mentioned below, yatren is an effective bactericide, whatever may be the position of the iodine or of the sulphonic acid group in the chinoline molecule. Therefore it would be interesting to definitely establish its constitution.

H. Höfling and R. Blum discuss the use of yatren in gynæcological practice. Höfling employed it in the form of 10 p. c. gauze, tampons, urethral or uterine bougies for the dry treatment of leucorrhœa. He cleansed and dried the vagina by means of pledgets of cotton wool and then plugged it with tryen gauze, using a speculum. With this procedure he took special care to ensure that the gauze also came in contact with the posterior part of the vault of the vagina. With this treatment, which was repeated twice or three times a week, the acute manifestations disappeared within a very short time. If the patients complained of a severe scalding sensation on the passage of urine, due to gonorrhœal urethritis, the introduction of a tryen urethral bougie, repeated two or three times, succeeded in removing the discomfort. The uterine bougies were used for the treatment of discharge from the cervix and uterine cavity. For the treatment of vaginal catarrhs Blum prefers the use of a mixture of 10 parts of tryen and 90 parts of talc. In mild cases this mixture is insufflated

* Compare Merck's Reports 1904 and 1905.

** Compare Merck's Reports 1893, 1894 and 1904.

Höfling, Allgemeine medizinische Zentral-Zeitung 1913, No. 18, p. 214.

Blum, Deutsche medizinische Wochenschrift 1913, No. 30, p. 1466.

once or twice daily, in severe cases three or four times a day, and the powder is removed a few days later by means of irrigations. This treatment proved effective in erosions of the portio and vagina, in acute gonorrhœa and in cancer of the uterus. The use of more concentrated mixtures or of pure tryen also yields good results in the treatment of wounds.

The bactericidal action of yatren likewise manifested itself in the treatment of diphtheria. H. Bischoff came to the conclusion that insufflations of yatren in diphtheria apparently shorten the permanent elimination of diphtheria bacilli, without causing any unwelcome secondary effects. He believes that the internal or subcutaneous exhibition of this preparation in typhoid fever might prove an effective means of combating the permanent elimination of bacteria. W. Kausch and F. S. Freund confirm the therapeutic value of yatren in the treatment of diphtheria. According to Freund it destroys the bacilli, even those situated in deep recesses and folds, and thus prevents the renewed formation of toxins. For this reason the preparation should be used simultaneously with the injection of antitoxin, and applied both internally and locally, as a prophylactic and curative. Its use should contribute towards hastening the healing process in streptococcal anginas. Internally 0.2 to 0.5 gramme (3—7½ grains) are given two or three times daily. The use of the preparation should be stopped if it causes too frequent evacuations of the bowels. Kausch also considers yatren a useful adjuvant to the treatment of diphtheria, in which it is useful as a prophylactic and curative in addition to the injection of antitoxin. It appears to be especially efficacious in the treatment of bacillus carriers. The author adhered in the main to the doses advocated by Freund; for children up to three years he prescribed single doses of 0.2 gramme (3 grains), and for children up to six 0.3 gramme (5 grains). He never saw any injurious effects which could be ascribed to the preparation, and he even believes that it exerts a beneficial influence on the kidneys. On the other hand, Evler states that tryen irritates the stomach, intestines and kidneys, and he demands

Bischoff, Deutsche medizinische Wochenschrift 1913, No. 38, p. 1834.

Kausch, ibidem 1913, No. 48, p. 2343.

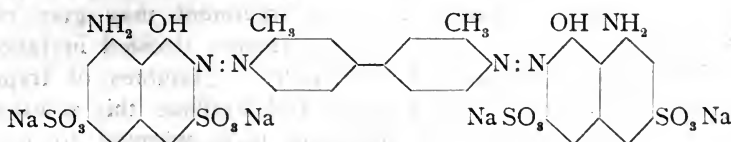
Freund, ibidem 1913, No. 48, p. 2341.

Evler, Therapeutische Monatshefte 1913, No. 9, p. 648.

that the maximum dose of the preparation should be determined prior to its further internal or external use.

Trypan Blue.

This blue dye, which is known under various designations such as diamine blue 3 B, benzo-blue 3 B, Congo blue 3 B, dianil blue H 3 G, naphthamine blue 3 B X, benzamine blue 3 B, azidin blue 3 B and Niagara blue 3 B, is issued in a pure form for medicinal use under the name of "trypan blue". It is the sodium salt of tolidin-disazo-bi-l-amido-8-naphthol-3, 6-disulphonic acid, of the formula:



Trypan blue occurs as a bluish-grey powder, which dissolves in water to a solution with a deep bluish-violet colour. It dissolves only in traces in alcohol, and is insoluble in ether and in chloroform. If 0.01 gramme is dissolved in 20 c.c. of water the colour of the solution changes to a pure blue on the addition of hydrochloric acid, and to reddish-violet on the addition of alkalis (solution of sodium hydroxide).

After Nuttall had used trypan blue with successful results in malaria in dogs, A. Theiler tried it in hæmaturia in cattle, likewise with successful results. Evers, Schwedesky and Zengel also confirm the high value of trypan blue treatment. They treated seven cases with subcutaneous injections of a 1 p.c. aqueous solution of trypan blue, all of which were cured within twenty-four to forty-eight hours, without the occurrence of any secondary effects. Evers advocates the subcutaneous application of trypan blue, since the latter is simpler and just as effective as intravenous injection. Almost all the trypanosomes in the animal's body are killed in the course of twenty-four hours and further danger is removed. Abscesses which may form at the site of injection can be incised without apprehension. The mucous membranes

Nuttall and Hadwen, *Parasitology* 1909.

Theiler, *Zeitschrift für Infektionskrankheiten, parasitäre Krankheiten und Hygiene der Haustiere* (Berlin) 1912, Vol. 11, p. 305.

Evers, Schwedesky, Zengel, *Berliner tierärztliche Wochenschrift* 1913, No. 24, p. 436.

of the animals treated with trypan blue are stained blue, and this coloration disappears of its own accord in the course of a fortnight. Evers emphasises the necessity of using the preparation at the earliest possible moment, since the animal dies as soon as 50 p.c. of the blood corpuscles has been destroyed.

Bergschicker reports that no deaths occurred among the cases in which trypan blue was used in the treatment of the above mentioned diseases, thus proving that this preparation is a sovereign remedy in piroplasmosis boum. Whereas Evers injected subcutaneously 100 c.c. of a 1 p.c. solution, notwithstanding that this treatment may give rise to the formation of abscesses, Bergschicker decided in favour of intravenous injection. He dissolves 3 grammes of trypan blue in 200 c.c. of distilled water and sterilises this solution; shortly before making the injection it is warmed to body temperature. The author maintains that the intravenous injection of this solution displays a prompter and more reliable action than its subcutaneous application. However, in no case did he observe any improvement until thirty-six hours had elapsed, and the urine did not become quite clear until the fourth day. His experience shows that trypan blue effects a cure even in comparatively severe forms of piroplasmosis within a short time, without producing any secondary effects, whereby it is superfluous to administer at the same time symptomatic remedies. The staining of the fingers caused by trypan blue can be removed by the use of chlorinated lime or hydro-sulphite.

Schnaudigel undertook intra vitam staining in rabbits by means of injections of trypan blue. After repeated applications he observed that the whole animal and the blood serum assumed a blue colour which persisted for a considerable time. In the eye a coloration of certain parts was seen.

Trypasafröl.

As is well known, L. Brieger and M. Krause, in continuation of Weber's investigations, undertook experiments with safranin in animals infected with trypanosomes, and

Bergschicker, Berliner tierärztliche Wochenschrift 1913, No. 28, p. 499.

Schnaudigel, Archiv für Ophthalmologie 1913, Vol. 86, No. 1.

Brieger-Krause, Berliner klinische Wochenschrift 1912, No. 31, p. 1453.

published their results*. On pursuing their investigations of substances belonging to the safranin group the authors found a particularly efficacious dye, to which they gave the name of "trypasafrol". Since the results of experiments on animals undertaken by these authors held out a hope that trypasafrol might prove useful in the treatment of trypanosomiasis in man, H. Ritz undertook chemotherapeutic experiments with trypasafrol.

Following the method of experimentation adopted by Brieger, after infecting mice and rats with *Trypanosoma Brucei* the dye was given internally in cakes; to guinea-pigs it was given mixed with minced turnips. From the published results of the author's experiments it is evident that even when given in the largest permissible doses trypasafrol did not possess any curative action in the experimental infection of the above mentioned animals by the strains of *Trypanosoma Brucei* used for this purpose. It is true that in mice a certain therapeutic influence was evident in that the course of the infection was slightly retarded by feeding with the dye. In guinea-pigs trypanosomes again occurred in the blood during the most energetic treatment. Therefore, the author's results are not in agreement with the results reported by Brieger and Krause, for which Ritz is unable to offer an explanation, although he surmises that the differences in the results may be due to variations in the strains used. However, he states that he also tried the use of trypanosan**, and in the control tests in which the latter was used, internally and subcutaneously, he obtained excellent curative effects, using the same strains. This dye has already been investigated by Röhl and Marks.

Trypsin.

As is well known, Beard proposed the use of trypsin for the treatment of cancer, in which it has been employed with more or less success***. F.W.Lamballe draws atten-

* Compare Merck's Report 1912, p. 375.

Ritz, Berliner klinische Wochenschrift 1913, No. 30, p. 1387.

** Compare Merck's Report 1912, p. 456.

Röhl, Zeitschrift für Immunitätsforschung 1909, Vol. 1.

Marks, ibidem 1909, Vol. 2.

Beard, Lancet 1905, No. 4249, p. 281. — Medical Press and Circular, December 20, 1905.

*** Compare Merck's Reports 1906, p. 250 and 1907, p. 249.

Lamballe, Medical Record, November 22, 1913.

tion to its use in combating malaria, in addition to quinine, especially when quinine is powerless to prevent recurrences. The author investigated its action in severe infections and relapses. Treatment consisted of intramuscular injections of trypsin and amylopsin*, for which a preparation of definite strength, supplied in ampoules, was used (the author does not state the name of the preparation); 1 c.c. of trypsin solution = 1250, and 1 c.c. of amylopsin solution = 500 Robert's digestive units. The contents of one ampoule of trypsin and of one ampoule of amylopsin, diluted with 8 c.c. of physiological salt solution, were injected for a single dose. One needle was used to aspirate the solution and another to make the injection and this precaution was taken so that none of the solution should penetrate into the cutaneous tissue where it might cause pain. Nevertheless an oedema persists for twelve to twenty-four hours at the site of injection. The injections displayed a marked effect, especially on the cerebral forms of malaria. The headache disappeared, the patients became calmer, the skin became moist, the temperature was reduced, and the patients' appearance changed already within a few hours and they became brighter and more cheerful. As a rule one injection sufficed to free the peripheral blood of parasites; in severe cases three injections, given at intervals of four days, are required. The author usually observed the occurrence of the "trypsin reaction" after three injections, i. e., a rise of temperature produced by trypsin which indicates that the patient is completely under the influence of trypsin. This method of treatment yielded very good results.

W. Baetzner states that surgical tuberculosis, or its conservative treatment, offers a further indication for trypsin injections. The solution of trypsin should not be warmed above 80° C. (otherwise it loses its efficacy) and should be injected subcutaneously into the immediate vicinity of the focus of disease. To allay the pain a little novocaine may be added. The author states that the injections, which can be repeated at intervals of five to seven days, exert a direct influence on the fungous substances which are rendered innocuous as

* Compare Merck's Report 1908, p. 341.

Baetzner, Practitioner 1913, Vol. 90, p. 203.

well as the tubercle bacilli. The patient's general health is likewise beneficially influenced by this treatment.

The property of trypsin in an alkaline solution of dissolving albumin, and its inhibition by the serum of pregnant women was used by H. Scholz for the diagnosis of pregnancy, as suggested by E. Rosenthal. For this purpose he employed the following reagents:

1. 0.1 gramme of trypsin is dissolved in 10–20 c. c. of physiological salt solution, 0.1 c. c. of normal solution of sodium bicarbonate is added and physiological salt solution is added to the mixture to make 100 c. c.

2. 0.2 gramme of casein is dissolved in 20 c. c. of $\frac{1}{10}$ normal solution of sodium hydroxide by gently heating, the mixture is neutralised with $\frac{1}{10}$ normal hydrochloric acid, using litmus as indicator, and physiological salt solution is added to make 100 c. c.

3. 5 c. c. of glacial acetic acid are mixed with 45 c. c. of absolute alcohol and 50 c. c. of distilled water.

To carry out the test 2 c. c. of casein solution and a mixture of 0.1 c. c. of the serum to be tested with 4.9 c. c. of physiological salt solution are placed into each of a series of test-tubes, whereupon trypsin solution is added to each test-tube in increasing amounts commencing with 0.1 c. c. and ending with 1.2 c. c. The contents of each test-tube are now made up to the same volume, the test-tubes are carefully shaken and placed for exactly thirty minutes in a thermostat. 2 or 3 drops of the mixture of acetic acid and alcohol are now added to the contents of each test-tube. The presence of non-digested casein produces a precipitate or turbidity. If the trypsin and casein solutions have previously been exactly standardised against each other (to determine the antitryptic index) the inhibition of digestion by the serum added points to the presence of pregnancy. In Scholz's experience this method is a useful supplementary test to the Abderhalden reaction*.

Scholz, Berliner tierärztliche Wochenschrift 1913, No. 48, p. 858.
Rosenthal, Zeitschrift für klinische Medizin 1911, Vol. 72.

* Merck's Reagenzien-Verzeichnis 1913, p. 1, Abderhalden-Schmidt's Reagens auf Eiweisstoffe und deren Abbauprodukte, or Merck's Report 1911, p. 443 and 1912, p. 304.

Uranoblen.

Since the preparations used for the local treatment of gonorrhœa are not always successful in killing the gonococci situated in the mucous membrane, as their action is not sufficiently penetrating, C. Bruck tried a new preparation of silver which, on account of its content of uranin (fluorescein-sodium), is capable of penetrating into the recesses of the mucous membrane. Therefore, the preparation, by fulfilling this requirement, is more effective than other remedies. The name of uranoblen has been applied to it, and according to Bruck it is a combination of silver and uranin with a content of about 40 p. c. of silver. It occurs as a reddish-brown powder, soluble in water. In an aqueous solution it is not precipitated by salts nor by albuminous substances. The solution displays a powerful bactericidal action which extends to a considerable depth, and is almost non-irritant. For the application of uranoblen the author adopts a method which he calls caviblen therapy. The method consists in the application of uranoblen (if necessary combined with the administration of antigonorrhœal remedies) by means of smooth, rigid, but thin-walled, capsules (caviblen bougies) which melt within a short time. These can be easily introduced, like a vulcanite bougie, into the anterior and posterior urethra, and contain the active substance in powder in a highly concentrated form. This method has the further advantage that the patient himself is able to introduce the bougie easily and without risk deep into the anterior urethra, while its introduction into the posterior urethra can be carried out by the practitioner as required. The capsules do not contain any fat and their mass is insignificant compared with that of the drug, so that the action of the preparation is not impaired by fats, as is the case with bougies made of cacao butter. The action is further enhanced by the fact that the preparation is deposited in concentrated form, as a powder, on the mucous membranes and dissolves in the urethral secretion. Bruck holds that caviblen therapy offers the best method of treatment at present available, both as regards efficacy and the practical absence of failures. This view is on the whole confirmed by A. Sommer and A. Glück.

Bruck, Deutsche medizinische Wochenschrift 1913, No. 43, p. 2073.

Sommer, Deutsche medizinische Wochenschrift 1913, p. 2075.

Glück, ibidem, p. 2076.

Ureabromine.

In the treatment of chronic alcoholism several symptoms such as protracted tremor, general bodily and mental unrest, conditions of excitement and of depression, anxious ill-humour, irritability and sleeplessness, often require a suitable remedy capable of replacing the alkaline bromides, the prolonged use of which is, as a rule, not tolerated, particularly in the presence of gastric complications. According to Buße ureabromine (calcium bromide urea) is indicated in these cases, since it displays a very good bromine action and may be given without apprehension in cases of impaired cardiac activity, disturbances of elimination, and irritability. In five cases of contracted kidney due to alcoholism associated with extreme restlessness, myodegeneratio cordis, marked tachycardia and arrhythmia, the author gave daily doses of 2 to 3 grammes (30—45 grains) with very gratifying results and without observing any unwelcome secondary effects. He states that ureabromine, in contradistinction to alkaline bromides, is very well borne by the severely affected gastric mucous membrane.

F. Johannessohn prescribed ureabromine with successful results in the treatment of epileptiform convulsions, nervous conditions of excitement of the heart, nervous sleeplessness, hysteria, neurasthenia, and hysterical convulsive seizures. In two cases of delirium tremens the patients became calmer, but the effect produced was insufficient, and the author believes that the doses given by him (1 gramme [15 grains] four times daily) were too small. A secondary effect, viz., bromine acne, occurred in one case only.

Mangelsdorf has used ureabromine in the treatment of epilepsy in adults — to some patients it was administered during a period of eight months — and he found that in 75 p. c. of the patients it still displayed the same anticonvulsive action as the alkaline bromides, even on its prolonged use. At the same time he saw a beneficial influence on the general health of the patients, showing that the heart is strengthened by the calcium component of the drug. The

Buße, Münchener medizinische Wochenschrift 1913, No. 47, p. 2624.
Johannessohn, Deutsche medizinische Wochenschrift 1913, No. 6,
p. 268.

Mangelsdorf, Psychiatrisch-neurologische Wochenschrift 1913, No. 47.

author was able to confirm the good action of ureabromine on the undesirable manifestations of bromism, already alluded to by other authors*.

Uzara.

Further reports on uzara, or uzaron**, have been published by O. Hirz, E. Frey, K. Justi and M. Wikker. The pharmacological investigations undertaken by Hirz yielded the following results: "the basic principle of the action of uzaron manifests itself in a gradual inhibition of all the processes of movement in organs with unstriated muscles, caused by irritation of the inhibitory end-organs of the sympathetic system". This mode of action of uzaron manifested itself on the annular and longitudinal muscular apparatus of the entire intestinal tract, and on the bladder, and was especially marked on the uterus. Compared with the analogous action of adrenalin, the effect of uzaron develops more slowly and is more lasting, therefore its use obviates the shock-like onset and very transient action of adrenalin. Uzaron also exerts a beneficial influence on spastic conditions of contraction, and this effect makes it possible to draw a further parallel, this time with the action of atropine, which in spite of its unwelcome secondary effects still remains the best remedy for vagotonic conditions. The author believes that uzaron may be used in several indications for atropine, without any drawbacks. A comparative study of uzaron and other remedies for dysentery showed that both simaruba and ipecacuanha do not possess a similar sedative effect on the intestinal movements. According to Guerber uzara is not only an antidiarrhœic but also an amœbicide, hence it may be expected to yield good results in the treatment of amœbic dysentery. Justi reports that Werner undertook trials in this disease, but without success. Justi himself treated five cases of amœbic dysentery by uzara. In three chronic cases practically no effect was evident, but in the other two cases he

* Compare Merck's Reports 1911 and 1912.

** Compare Merck's Reports 1911 and 1912.

Hirz, Archiv für experimentelle Pathologie 1913, Vol. 74, p. 318.

— Münchener medizinische Wochenschrift 1913, No. 40, p. 2220.

Frey, Münchener medizinische Wochenschrift 1913, No. 8, p. 441.

Justi, ibidem 1913, No. 14, p. 765.

Wikker, ibidem 1913, No. 50, p. 2808. — Praktitscheski Wratsch 1913, No. 28.

obtained a complete success. Uzara appears to display a prompt action likewise in bacillary dysentery. Justi reports one case in which the customary remedies, such as kaolin and injections of gelatin, had failed and which was quickly cured by uzara. In other cases uzara did not prove superior to the other specific remedies, and in two severe cases it failed entirely. Therefore, too much should not be expected when prescribing uzara, since the hopes placed by the patients in the drug may be doomed to disappointment.

Wikker states that uzara has a marked astringent action which should prove useful especially in acute and subacute, in a lesser degree in chronic, forms of diarrhoea. With regard to its action on blood pressure and the difference between the action of uzara and that of opium the papers by Hirz and Frey should be consulted.

Valamin.

According to C. Lewin, valamin is the isovalerianic acid ester of amylene hydrate, and occurs as a clear liquid, with a neutral reaction, which is only slightly soluble in water. It has the formula $(\text{CH}_3)_2\text{C}_2\text{H}_5\cdot\text{COOC}_5\text{H}_9$. The preparation has a faintly aromatic odour and taste, resembling valerianic acid, and is supplied in capsules containing 0.25 grammes.

Lewin demonstrated the harmlessness of comparatively large doses of valamin in experiments on animals. He found that the preparation is very slowly split up in the intestines of the animals, so that the amylene hydrate which is liberated does not display a hypnotic action. The author assumes that in man the preparation is absorbed in the stomach, since valamin is not decomposed by the acid gastric juice and the sedative effect sets in so quickly that in his opinion it can scarcely be ascribed to its decomposition in the intestines.

The therapeutic investigation of valamin undertaken by Simonsohn, Zahn and Kaiser, G. Thalheim and Bräutigam shows that the preparation is well borne and yields

Lewin, Therapie der Gegenwart 1913, No. 4, p. 162.

Simonsohn, Allgemeine medizinische Zentral-Zeitung 1913, No. 37, p. 437.

Zahn-Kaiser, Medizinische Klinik 1913, No. 46, p. 1894.

Thalheim, Therapie der Gegenwart 1913, No. 12, p. 571.

Bräutigam, Deutsche medizinische Wochenschrift 1913, No. 47, p. 2302.

good results, as a sedative and hypnotic, in neurasthenic and depressive conditions of excitement, nervous insomnia, gastric neuroses, hysteria and convulsive states of the bronchi. Bräutigam used it with successful results to combat conditions of fear on the evening before operation. Some of the above cited authors complain of the smell of valerianic acid of the preparation; recently, however, this has been masked to such an extent that the patients no longer object to taking the drug. In most cases two to four capsules will be found sufficient, i. e., 0.5 to 1 gramme of valamin.

Validol.

Kendall discusses the value of validol in vomiting due to pregnancy or to sea-sickness. The latter is caused by stimulation of the vagus and the vomiting is due to reflex action and is the symptom which causes the patient the greatest discomfort. The author does not consider bromine, or the use of bromides, to be suitable for combating the reflex vomiting since it readily gives rise to nausea, and the same applies to menthol which, although useful, has an irritant action. On the other hand, validol (valerianic acid menthol ester) is free from this drawback, and yields the desired result by reason of its action on the gastric mucous membrane and on the naso-pharynx. Kendall holds that as is the case in sea-sickness vomiting in pregnancy is also due to a disturbance of the regulatory centre and can be beneficially influenced by a remedy with an analgesic effect, such as validol. In agreement with other authors* he also obtained good results with this preparation. If it is desired to administer bromine at the same time, the following tablets may be prescribed:

Rp. Sod. brom.	5 grammes (75 grains)
Magnes. lev.	2 „ (30 „)
Validol.	2 „ (30 „)
Ft. tabl. x.	

Before starting on the journey one or two of these tablets should be taken, and if necessary one tablet may be taken every hour, up to four tablets daily.

Kendall, Medical Press and Circular 1913, No. 3843 and 3848.

* Merck's Report 1905, p. 214.

M. Neubauer confirms an observation already made by Sbordone that validol possesses an anthelmintic action. He gave it with successful results in pavor nocturnus in children, and found that the manifestations due to oxyuris also disappeared. He states that according to the age of the child 2 to 10 drops of validol are given once or several times daily, in a little sugar and water.

Veronal and Veronal-Sodium.

O. Grisslich discusses the subject of veronal treatment* in patients who have been taking the drug for several years. He was able to observe the action of veronal in a man, aged 78, for whom he had prescribed veronal for three years. The patient suffered from peripheral arterio-sclerosis, myodegeneratio cordis, contracted kidney and prostatic enlargement; the unbearable pains of the bladder caused by the latter made it necessary to resort to catheterization several times day and night. This condition lasted for three years during which veronal, given in doses of 0.45 to 0.75 gramme (7—11 grains), proved very useful. It exerted a beneficial influence on the psychic depression, the severity and hopelessness of the malady, and never failed. The patient's insomnia could usually be combated by taking 0.5 gramme ($7\frac{1}{2}$ grains) of veronal before going to bed, and its action lasted until 4 or 5 a. m. No habituation to the drug occurred. Trional, sulphonal and paraldehyde failed. A point of special importance in connexion with this case is the fact that in the three years during which veronal was administered no harmful secondary effects were seen either in regard to the bodily functions or to the patient's mental state. Veronal exerted no deleterious effect on the kidneys or organs of circulation, nor was a cumulative action seen. The patient, who was mentally very active up to the time of his death, had taken during the three years in all 422 grammes (15 oz) of veronal, as a hypnotic and sedative. The smallest active dose was 0.2 gramme (3 grains), and the largest 0.75 gramme (11 grains). Basing on the observations made in this case Grisslich feels justified in recommending the prolonged use of veronal in the same patient in suitable cases.

Neubauer, Deutsche Medizinal-Zeitung 1913, No. 50, p. 795.

Grisslich, Medizinische Klinik 1913, No. 46, p. 1895.

* Compare Merck's Reports 1903—1912.

Rixen also frequently had occasion to confirm the beneficial influence of veronal on the general condition of the patients. Persons in a state of extreme excitement and who suffered bodily and mentally from want of sleep were scarcely recognizable after profound sleep had been induced two or three times by the administration of veronal. The author never saw any deleterious effect on the heart or kidneys; in a few cases he found that veronal displayed its full hypnotic effect on the second night following its administration. In persons who have not made use of soporifics Rixen begins with 0.25 to 0.3 gramme (4—5 grains), given in hot tea, and when this amount no longer displays a sufficient action the dose is increased to 0.5 gramme ($7\frac{1}{2}$ grains). The author does not repeat this dose on more than three consecutive nights, without first allowing an interval.

W. House achieved very good results with veronal in psychiatric practice. Doses of 0.5 to 1 gramme ($7\frac{1}{2}$ —15 grains) sufficed to induce sleep; susceptible patients slept for twelve hours and longer after these amounts. In older persons and after the prolonged use of veronal the author saw slight vertigo, which quickly disappeared after the morning cup of coffee. After the prolonged use of veronal some patients experienced weakness in the legs and lessening of physical activity. In some cases the urine became scanty and dark, but the author never found albumin or sugar in the urine. He states that veronal fills all the indications which in past years were met with chloral, but with infinitely less danger. Its realm includes the insomnia of neurasthenia, psychasthenia, alcoholism, mania, paresis, morphinomania, hysteria, chorea, and vomiting of pregnancy. House states that the use of veronal is contra-indicated in acute nephritis and in extensive heart disease, especially in aortic regurgitation. Chronic nephritis is not a contra-indication to moderate occasional veronal dosage. Toxic symptoms were observed only after a single dose of 2 grammes (30 grains). The author does not state how long veronal may be given, but he reports a case in which it was taken for a prolonged period without ill effects. The case was that of a physician who took veronal in 0.3 to 0.6 gramme doses (5—10 grains) almost every night

Rixen, *Ärztliche Rundschau* 1913, No. 8, p. 87.

House, *Therapeutic Gazette* 1913, Vol. 37, No. 5, p. 327.

for more than a year without ill effects, and at the end of that time, having recovered from his neurasthenic state, was able to discontinue it without effort. Another physician, however, who had taken veronal for several months suffered great discomfort on leaving off the drug. When the urine is dark House gives spirit of nitre and potassium acetate in small doses, and the dark urine quickly disappears. Veronal appears to be incompatible with calomel if both are administered near together.

The form in which veronal is given is not without bearing upon its action. Grisslich emphasises the necessity of giving veronal in solution; House and Rixen prefer the use of powder to that of tablets. Rehm hastens the onset of the action by directing his patients to chew the tablets, and to take the drug earlier than is usual. By this means it is possible to obviate the dizziness which is sometimes present on awaking. Veronal should not be taken late at night, but if this cannot be obviated veronal-sodium should be taken, which is readily soluble and quickly absorbed and therefore displays a somewhat prompter action.

C. Bachem points out that veronal has proved useful as a sedative before operations. For this purpose a fairly large dose is given on the evening before the operation, or the drug is given prior to chloroform anæsthesia. The value of this combined method is apparent from the fact that vomiting occurred in only 2.3 p. c. of cases, and that anæsthesia was induced already after two and a half minutes, and that a deleterious influence on the pulse was scarcely ever noted. Schlimpert advocates the administration of veronal on the evening before sacral anæsthesia.

Thiemich states that children suffering from disturbances of metabolism require as much sleep as possible, and he considers it advisable to arrest the threatening loss of strength by artificially induced sleep. If a hypnotic is to be used for this purpose, such as veronal, veronal-sodium or chloral hydrate, the author states that basing on his experience it is useless to administer the homœopathic small

Rehm, Psychiatrisch-neurologische Wochenschrift 1912, p. 75.

Bachem, Berliner Klinik 1913, No. 299, p. 2.

Schlimpert, Surgery, Gynecology and Obstetrics, May, 1913; Lancet 1913, II, p. 1855.

Thiemich, Fortschritte der Medizin 1913, No. 22.

amounts advocated by the cautious compilers of prescription booklets as the doses for infants. On the other hand, to avoid an overdose chloral hydrate should be given in an aqueous solution in divided doses. For this purpose at first two teaspoonfuls of a 1.5 p. c. solution of chloral hydrate, sweetened with saccharin, are given, followed by one teaspoonful every 15 or 20 minutes. The author tried veronal-sodium in children under one year and found 0.1 gramme ($1\frac{1}{2}$ grains) a sufficient and at the same time harmless single dose. In isolated cases in which the action was insufficient he again gave 0.05 gramme ($\frac{3}{4}$ grain) once or twice, at intervals of half an hour.

W. Hildebrandt's communications regarding the value of veronal in pulmonary tuberculosis are particularly interesting. Veronal is an ideal remedy in the night sweat of incipient tuberculosis associated with hectic fever. It is administered alternately with trional in doses of 0.25 to 0.5 gramme (4 to $7\frac{1}{2}$ grains), dissolved in a warm beverage. In some cases a permanent success, i. e., the disappearance of the night sweat, is obtained by a single dose; as a rule, however, this treatment must be continued for some time, giving the drug in the evening every second or third day; in terminal phthisis it must be continued permanently. Since the action of the drug frequently extends over several days, it is advisable to suspend its use from time to time. Veronal treatment is especially useful in terminal phthisis, in the first place since it causes the disappearance of the night sweat, and secondly in that it induces a quiet, refreshing sleep. Hildebrandt states that with this treatment the action on the night sweat scarcely ever fails, and is unsatisfactory only in moribund patients.

Pharmacological investigations of veronal and other hypnotics have been undertaken by F. Engelhardt and C. Siegfried. Engelhardt found that veronal is a powerful hypnotic which, given in appropriate doses, induces in the experimental animals prolonged sleep, without harm to the organism. Siegfried undertook a clinical study of the action of veronal, luminal and isopral. He found that doses of 0.75

Hildebrandt, Zeitschrift für ärztliche Fortbildung 1913, No. 12, p. 366.

Engelhardt, Dissertation Berlin 1913.

Siegfried, Dissertation Leipzig 1913.

gramme (11 grains) of veronal almost invariably produced a fall of blood pressure. Small doses of 0.2 gramme (3 grains) of luminal displayed the same effect in about 50 p.c. of cases, while small doses of 0.5 gramme (7½ grains) of veronal produced a rise of blood pressure in nine cases, and a fall in one case. Doses of 2 grammes (30 grains) of isopral always produced a fall of blood pressure, with 1 gramme (15 grains) this occurred in about 50 p.c. of the cases.

A. Gregor also undertook experiments with various hypnotics with a view to studying their action on the pulse and blood pressure. In view of the results of his tests on women he is unable to endorse unreservedly the statements in the literature regarding the harmlessness of veronal, as he frequently saw a marked deleterious influence on the cardiac activity even with moderate doses.

Cases of idiosyncrasy to veronal, and toxic effects referable to this hypnotic, are reported by G. Pernet, Ch. Vallon, R. Bessière, H. J. Rossello, Rommel, W. H. Willcox and K. Tholl. A distinction must be made between toxic secondary effects which occasionally occur on account of idiosyncrasy to the drug, and those which may occur on prolonged use (veronal habit), and toxic effects produced by a deliberate or accidental overdose (taken with suicidal intent). Willcox states that in acute poisoning in consequence of an overdose deep sleep with marked rise of temperature is present, which may end in death in coma and with the clinical signs of pneumonia. Frequently slight nephritis and scarlatini-form eruptions occur. In cases of chronic poisoning hallucinations, tremor, ataxia, and disturbances of sight, gait and speech occur. Therefore, to prevent accidental and deliberate poisoning by veronal, Willcox urges that it should be dispensed only on a medical practitioner's prescription, and its administration should be supervised by the medical attendant. This restriction on the sale of veronal is already in existence in several countries, and it may be assumed that cases of poison-

Gregor, *Monatsschrift für Psychiatrie und Neurologie* 1912, Vol. 32, p. 54.

Pernet, *British Medical Journal* 1913, II, p. 312.

Vallon-Bessière, *L'Encéphale* 1913, Vol. 8, No. 3, p. 245.

Rossello, *Semana médica* 1913, Vol. 20, No. 1019, p. 202.

Rommel, *Charité-Annalen* 1912, Vol. 36, p. 62.

Willcox, *Lancet* 1913, II, p. 1178.

Tholl, *Dissertation Bonn* 1912.

ing due to ignorance of the action and dosage of veronal have been reduced to a minimum. Nevertheless, the treatment of cases of poisoning by veronal is a matter of interest to the practitioner. Willcox maintains that washing out of the stomach is the only effective method of treatment, and should be carried out within the first five or six hours. Rommel advocates, in addition to gastric lavage, the use of cardiac stimulants and of adrenalin, but deprecates the use of infusions of sodium chloride, as the latter merely impose a further burden on the circulation. On the other hand, Tholl found that adrenalin (and strychnine) failed entirely. In mild cases camphor may be used, but acetic ether and caffeine yield the best results.

Mention may still be made of a communication by M. Page dealing with a rational method of treating morphinism, in which the use of veronal and ammonium valerianate as adjuvants plays a certain rôle*.

Vioform.

For the dry treatment of venereal ulcers E. J. Goldberger recommends the use of vioform** (chloro-iodo-oxy-chinoline), which is especially suited for this purpose on account of its antiseptic, antipyretic and antifermentative properties. The author states that in hard ulcers it displays a double action, in the first place it removes the mixed infection within a surprisingly short time, and also exerts a beneficial effect on the ulcer itself in that it stops the discharge, reduces the infiltration in its vicinity and stimulates granulation. According to Goldberger the hardening of the ulcer under the influence of vioform is of diagnostic value, since a similar action of vioform is never seen in the case of non-venereal ulcers. In the treatment of venereal sores vioform is applied in a thick layer and kept in place by means of a suitable dressing.

L. Robraz has used vioform in the treatment of suppurating wounds, leucorrhœa, fistulas, tuberculosis of the bones, and in the post-operative treatment of these affections, and

Page, *Annales médico-psychologiques* 1913, Vol. 10, p. 532. —
Thérapeutische Monatshefte 1913, No. 8, p. 615.

* Compare Merck's Reports 1906, p. 259 and 1911, p. 451.

Goldberger, *Dermatologische Wochenschrift* 1913, No. 50, p. 1468.

** Compare Merck's Report 1905, p. 218.

Robraz, *La clinique* 1912, No. 51.

he found that healing ran a quick and smooth course. Besides being absolutely non-toxic it also has an analgesic action, which makes it particularly useful in children's practice. For the treatment of wounds he prescribed vioform mixed with 30 parts of vaseline or with 15 parts of collodion, or a mixture of equal parts of vioform and sterile powdered wood charcoal. In coryza he prescribed an ointment consisting of 0.2 gramme (3 grains) of vioform, 0.05 gramme ($\frac{3}{4}$ grain) of menthol, 0.1 gramme ($1\frac{1}{2}$ grains) of stovaine, and 15 grammes ($\frac{1}{2}$ oz) of vaseline; of which an amount the size of a pea is introduced every evening into each nostril. In psoriasis a mixture of 5 grammes of absolute alcohol, 4 grammes of chrysarobin, 4 grammes of pyrogallie acid, 0.5 gramme of vioform, and 90 grammes of collodion yields good results. P. Fedoroff also expresses a very favourable opinion of the value of vioform as an antiseptic in the treatment of wounds.

J. Hochstätter records the results of vioform treatment in dermatological practice. In balanitis with considerable hyperæmic inflammation of the glans penis healing usually set in within three days under the application of a 10 p.c. ointment. The use of a 5 p.c. ointment proved equally effective in intertrigo. The application of vioform powder yielded good results in the treatment of diabetic pruritus, iodoform eczema, eczema of the skin, and in fissures of the rectum. In *ulcus durum* and *molle* the author employed vioform in powder form with good results, like Goldberger, and if the action proved insufficient he prescribed the following mixture: Rp. Vioform 2 grammes (30 grains), menthol 0.5 gramme ($7\frac{1}{2}$ grains), camphor 1 gramme (15 grains), ung. simpl. 30 grammes (1 oz). The wound heals best if this ointment is applied three times daily.

Xanthydrol*.

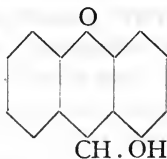
Xanthydrol, also called diphenopyranol, or according to A. Baeyer's suggestion xanthanol, occurs in the form of microscopical needles which, with the exception of alcohol, are insoluble or almost insoluble in the customary solvents.

Fedoroff, *Therapeutischeskoje Oboshrenie* 1913, No. 18, p. 569.

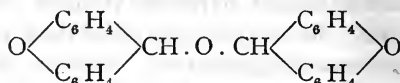
Hochstätter, *Dermatologische Wochenschrift* 1913, No. 10, p. 282.

* Compare R. Meyer and E. Saul, *Berichte der deutschen chemischen Gesellschaft Berlin* 1893, Vol. 26, p. 1276 and Graebe, *Annalen der Chemie und Pharmazie* 1889, Vol. 259, p. 280.

It dissolves in boiling ligroin, from which it crystallises out on cooling. However, the longer it is heated the more of it is converted into the ether of xanthydrol.



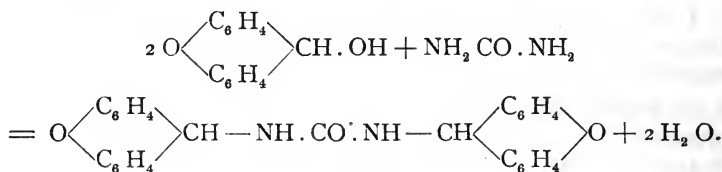
Xanthydrol



Ether of Xanthydrol

Xanthydrol dissolves in concentrated sulphuric acid forming a solution with a yellow colour and green fluorescence. Melting point 120° — 122° C.

With primary amines and diamines xanthydrol forms compounds, with formation of water, of which the condensation product of xanthyl and urea is particularly interesting:



This compound, dixanthyl urea, forms white needles, which melt at 264° C. with decomposition. It is not acted upon by caustic alkalis; it is insoluble in water and with difficulty soluble in hot alcohol*. For this reason xanthydrol can be used for the quantitative estimation of urea, and this method of precipitating urea should prove especially useful in physiological investigations. L. Hugouneq and A. Morel have made an exhaustive study of this method, and these authors describe a method by means of which the content of urea in physiological solutions such as urine and serum can be easily and accurately estimated by the gravimetric method. For this purpose 10 c. c. of serum, for instance, are mixed with 10 c. c. of alcohol (95 p. c.) and the mixture is acidulated with acetic acid. The coagulum thus obtained is brought on a filter and after the liquid has filtered through it is twice washed with two successive portions of 10—20 c. c. of

* Compare R. Fosse, *Comptes rendus de l'académie des sciences* 1906, Vol. 143, p. 749 and 1907, Vol. 145, p. 813.

Hugouneq-Morel, *Presse médicale* 1913, No. 52, p. 517.

alcohol. The filtrate, which contains the urea, is evaporated down in a glass capsule to about 5 c. c., whereupon 50 c. c. of a 5—8 p. c. alcoholic solution of xanthidrol, and then 50 c. c. of glacial acetic acid are added. The mixture is allowed to stand at ordinary temperature for four hours, when the dixanthyl urea separates out. It is collected in an Allihn tube, dried at 105° C. and weighed. The weight found is divided by 7 and the resulting figure indicates the amount of urea contained in the amount of serum employed for the test. For washing out the dixanthyl urea the authors used an almost saturated alcoholic solution of dixanthyl urea, until the disappearance of the acid reaction. It may be mentioned that the Fosse test is specific for urea, for other substances present in the juices of the body, such as glycoll, alanine, leucin, tyrosin, glutamic acid, cystin, lysin, histidine, tryptophan, etc., do not give this reaction under the above described conditions.

Xylol.

The great importance which benzol seems destined to attain as a remedy in leukæmia* draws attention to its homologues which may also prove of therapeutic interest. Thus we know that Zuelzer recommended the use of xylol (dimethyl benzol = $C_6H_4 \cdot CH_3 \cdot CH_3$) for the treatment of small-pox. As was reported some years ago by Wischnewsky, Belin and Teissier, the internal administration of this drug has proved useful. Pawlowski states that it yields good results in typhoid fever. According to a recent communication by Missikow, xylol, applied externally, displays an antiseptic action which may prove useful in the treatment of skin diseases, e. g., in scabies, as the author found that xylol quickly kills parasites and also insects. His trials with xylol in the treatment of scabies yielded very gratifying results. The preparation rapidly penetrates into the skin and evaporates very quickly so that it cannot produce any injurious effects; nevertheless, it displays an excellent action in that it immediately kills all the mites. On account of its bactericidal and

* Compare the article on Benzol in this Report.

Zuelzer, Wischnewsky, Belin, Teissier, Merck's Report 1905, p. 229.

Pawlowski, Merck's Report 1909, p. 345.

Missikow, Therapieitscheskoje Oboshrenie 1913, No. 4.

desiccating properties the application of xylol also proved successful in eczema, and in onychomycosis favosa and herpes tonsurans.

Yeast.

Biozyme was already investigated by K. Seegers, who stated that it was a good preparation, displaying the same effect as fresh yeast. This is borne out by A. Stephan, who found that the preparation resembled fresh yeast in regard to its chemical composition, content of zymase and fermentative power. He also points out that this preparation is distinguished by its keeping properties. Its indications are the same as for yeast; as far as I am aware no papers dealing with its uses have been published*.

Fermentin. This preparation of yeast was used by J. Hirschfeld in the form of tablets (of 1 gramme) in the treatment of the vagina. He first cleansed the cervix and vagina by means of cotton wool and then introduced a fermentin tablet with a dressing forceps directly in front of the external orifice of the uterus. The tablet is kept in position by a plug of cotton wool impregnated with glycerin. After twelve hours the plug is removed and the vagina is irrigated with an astringent solution. The tablets were applied daily, or every second day. They are non-irritant and afford a useful and simple means of treating catarrhs of the vagina and cervix. The tablets are also useful in the treatment of severe inflammatory diseases of the female organs in which they display a symptomatic effect and allay the troublesome symptoms attending the catarrh and the leucorrhœa.

Furunculin. R. Polland reports on the internal and external application of this preparation. Given per os it proved especially useful in furunculosis. It is more difficult to judge the value of yeast in acne juvenilis and in the maladies associated with seborrhœa, however, the author believes that a trial is justified if in young people the disease is accompanied by excessive fermentation in the intestines. The author

Seegers, Merck's Report 1912, p. 467.

Stephan, *Therapeutische Monatshefte* 1913, No. 5, p. 356.

* See the articles on Yeast in Merck's Reports 1899—1912.

Hirschfeld, *Fortschritte der Medizin* 1913, No. 22, p. 606.

Polland, *Therapie der Gegenwart* 1913, No. 3, p. 116.

tried the external use of furunculin paste in the treatment of eczemas, especially in impetiginous eczema associated with suppurating pustules. A thick layer of the paste on linen was applied to the affected areas, and already after a few hours fermentation took place and the dressing could be replaced by an ointment. This treatment was repeated on the following day. The results were encouraging. Furunculin, like all preparations of yeast, yields good results in the treatment of catarrhs of the vagina and cervix. In these cases the preparation is applied in powder form on cotton wool, and removed after a few hours, whereupon the vagina is irrigated. N. Galdonyi prescribed furunculin paste and furunculin soap with gratifying results in furunculosis and in wounds caused by riding. A. Dutoit used it in various diseases of the eyes. In blepharo-conjunctivitis on a scrofulous basis he gave furunculin powder internally and applied externally furunculin paste and furunculin powder, and with this treatment achieved in every instance a cure and an improvement of the general condition. The same success was obtained by internal and external furunculin treatment in scrofulous kerato-conjunctivitis, catarrhal corneal ulcers, herpes corneæ febrilis and anterior episcleritis. In two cases of scleritis and sclerotic keratitis a clearing up of the long standing corneal opacities was obtained by the use of furunculin paste and massage. Since furunculin is well borne by the cornea and conjunctiva, both in powder and paste form, the author considers it a useful remedy for the treatment of diseases of the eye, especially those of an eczematous character.

Levurinoſe. In *acne juvenilis*, if the intestinal functions are in order, E. Baumer prescribes the use of levurinoſe soap only, the action of which may be intensified by the addition of sulphur and salicylic acid. However, as soon as the stools become irregular he also gives levurinoſe per os, in doses of one heaped teaspoonful, three times daily. If the use of levurinoſe soap alone should prove ineffective, recourse must be had to pastes producing exfoliation, while larger pustules are opened. Of course, a suitable diet must be prescribed. The author also obtained good results by the internal

Galdonyi, Wiener medizinische Wochenschrift 1913, No. 26.

Dutoit, Archiv für Augenheilkunde 1913, Vol. 74, No. 3—4.

Baumer, Medizinische Klinik 1913, No. 16, p. 628.

administration of the preparation in the treatment of furunculosis.

Xerase. O. Abraham deals with the xerase treatment of leucorrhœa, in succession to his former communications on this subject*. In the place of capsules of xerase he now uses xerase tablets (1.5 grammes each), which can be easily introduced into the vagina where they rapidly disintegrate. To mask the foul odour which xerase assumes in the vagina the author prescribes the addition of oil of cloves to the tablets, whereby their action is not impaired but the foul smell is very considerably reduced. His xerase treatment is now carried out as follows: 5 to 8 grammes of xerase powder are introduced into the vagina by means of a speculum twice a week, and is washed out 8 to 24 hours later by means of infusion of chamomile. On the other evenings during the week the patient is directed to introduce herself, as deep as possible, one xerase tablet, and to remove the residue on the following morning by irrigating with infusion of chamomile. Basing on the results of his extensive trials the author states that xerase treatment is indicated in gonorrhœal colpitis, erosions, catarrhs of the cervix, and in catarrhal colpitis in which no gonococci have been found. Cases of colpitis and erosions were cured without exception within a short time, after three to fifteen applications of xerase. Only about 10 p.c. of the cases of catarrh of the cervix required further intra-uterine treatment. Xerase also proved useful in some cases of vulvo-vaginitis in little girls. In these cases the author introduced the preparation either in powder form or in the form of bougies prepared with tragacanth.

Zinc Sulphate.

M. Kashiwabara was led to investigate the usefulness of zinc sulphate as a precipitant of uric acid on the basis of an observation reported by Kojo. As a result of his investigations he elaborated the following method for the estimation of uric acid.

100 c. c. of urine of average concentration are made alkaline by the addition of a few drops of solution of sodium carbonate,

Abraham, Berliner klinische Wochenschrift 1913, No. 23, p. 1065.

* Compare Merck's Report 1910, p. 180 and 1911, p. 454.

Kashiwabara, Zeitschrift für physiologische Chemie, Vol. 84, p. 222.

Kojo, *ibid.*, Vol. 73, p. 416.

whereupon solution of zinc sulphate (10 p. c.) is added until it no longer causes a precipitate; to this end about 30 c. c. are required. The acid reaction produced during precipitation is converted into a faintly alkaline reaction by the addition of solution of sodium carbonate. After standing for half an hour to one hour, or longer, it is filtered, the precipitate is collected quantitatively and washed with distilled water until no turbidity is produced on the addition of solution of barium chloride to the washings, after acidulation with hydrochloric acid. The filter is now pierced and the precipitate is washed into a flask by the use of 150—200 c. c. of water, a few c. c. of 30 p. c. acetic acid are added and the precipitate is decomposed by passing in sulphuretted hydrogen, whereupon the contents of the flask are heated to boiling, filtered while hot and washed out. The filtrate and the washings are evaporated down on a water-bath to a few c. c., about 5 to 8 drops of hydrochloric acid (sp. gr. 1.126) are added and the uric acid which separates out is weighed on the following day either on a tared filter or in a Gooch crucible.

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